THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 71 MAY, 1954 No. 5

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INTRALOBAR BRONCHOPULMONARY SEQUESTRATION

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TO OUR knowledge at the time of this writing there have been 79 surgical cases of intralobar bronchopulmonary sequestration.

In 1950, we reviewed the literature on intralobar bronchopulmonary sequestration,[3] and presented 5 cases from the surgical service of one of us (Clagett). With these 5 cases we were able to collect 39 surgical cases. Since that report a number of papers on this subject have appeared in the literature. Owing to the prevailing awareness of this condition, its embryologic interest and surgical importance, and because it presents a definite and often recognizable syndrome, we are reviewing some aspects of the literature on the subject since 1950, and reporting 5 more cases from the files of the Mayo Clinic. Again, we have included only cases in which the only thoracic defects present were the anomalous artery and pulmonary anomaly and in which operation was performed.

By the term "intralobar bronchopulmonary sequestration" is meant a partial or complete developmental separation of a portion of a lobe of a lung from its continuity with the normal bronchial tree. In this so-called sequestered portion of pulmonary tissue, congenital cystic disease of the lung occurs. The adjective "intralobar" is used to differentiate the condition from "extralobar" sequestration. In extralobar sequestration, an anomalous, nonfunctioning piece of pulmonary tissue is found either below the diaphragm or between the diaphragm and the lower lobe. The sequestered pulmonary tissue in cases of intralobar sequestration lies enclosed within the pleura of the involved lower lobe whereas in cases of extralobar sequestration the sequestered pulmonary tissue is enclosed in a

pleural sheath of its own. The embryologic basis for the two conditions is likely to be rather similar.

The etiologic factor in intralobar sequestration is, according to present consensus, as first put forward by Pryce and associates,[21,22] an anomalous artery that arises from the lower part of the thoracic or the upper part of the abdominal aorta or from one of the branches of the celiac axis. This artery enters the affected lower lobe, usually by way of the pulmonary ligament. Beneke, arguing that sequestered tissues develop and obtain their own blood supply, put forward the view that the pulmonary sequestration is a primary developmental anomaly, and that the anomalous blood supply is secondary. However, as pointed out by Pryce, cases have been encountered in which an anomalous artery from the aorta supplies one or both lower lobes, such lobes being otherwise normal and containing no sequestered tissue. Such a case was described by Natucci. In it, both lower lobes of the lungs were supplied by anomolous arteries from the aorta, and these lobes were otherwise anatomically normal. In other words, the anomalous vessels were not secondary to a pulmonary abnormality. It is, therefore, much more reasonable to assume, as suggested by Pryce, that if the pulmonary anomaly is present as well, it is secondary to the vascular anomaly.

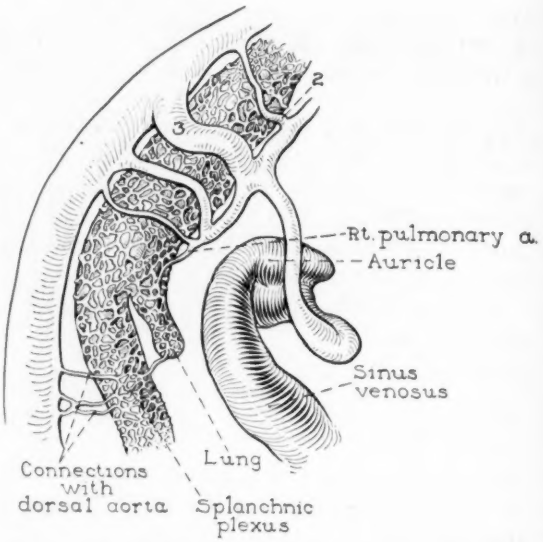

FIG. 1. Connections of dorsal aorta to splanchnic plexus and pulmonary plexus. Persistence of these connections is thought to be responsible for the anomalous artery in cases of intralobar bronchopulmonary sequestration. Reprinted with modifications (by permission) from Bruwer, André, Clagett, O. T., and McDonald, J. R. Anomalous arteries of the lung associated with congenital pulmonary abnormality. *J. Thoracic Surg.*, 1950, *19*, 957–972.

EMBRYOLOGY AND PATHOGENESIS

In the earliest stages of fetal development the embryonic gut is covered by a vast plexus of vessels called the "splanchnic plexus."[2] This plexus has connections with the dorsal and ventral aortas.[4] When, at the 3 or 4 mm. stage, the pulmonary anlage buds from the primitive foregut, it carries with it part of the splanchnic plexus. This part has been called by Huntington the "postbranchial pulmonary plexus." Into this plexus the pulmonary artery, which develops from the sixth primitive aortic arch, inosculates, and so establishes the pulmonary arterial network. If, for some reason, one or more of the connections between the dorsal aorta and the postbranchial pulmonary plexus persist (Fig. 1), the result is thought to be one or more anomalous arteries from the aorta to the pulmonary lower lobes. Pryce stated that these persisting arteries, by traction on the developing buds of the lower lobe which they supply, may cause some of these buds to be separated from their normal bronchial connections. These separated portions do not function after birth, and are liable to form cysts and become infected.

In the great majority of cases reported, the sequestered pulmonary tissue has been in the posterobasal segment of a lower lobe. This constant location is probably indicative that the abnormality occurs at a rather uniform time in the embryologic development of the lung and its vascular system in this region. Cases have been reported, however, in which the sequestered tissue was in a somewhat different anatomic location. In a case reported by Tosatti and Gravel, a large cyst was demonstrated in the apical segment of the right lower lobe. In a case reported by Findlay and Maier, agenesis of the right lower and middle lobes of the lung was demonstrated with anomalous arteries passing through the diaphragm to the upper lobe. Two cysts were located in the upper

lobe. There were no normal pulmonary arteries or veins on this side. The fact that there was a right upper lobe, in the absence of a pulmonary artery or vein to it, albeit not a normal lobe, supports statements such as that of Meschan and Calhoun who said: "It is also open to discussion as to whether the defect in bronchopulmonary hypogenesis may be primary in the pulmonary vascular system rather than in the respiratory system."

Without doubt a close relationship frequently exists between developmental abnormalities of the pulmonary vessels and the respiratory tree. Cole and his co-workers mentioned the work of Pryce, but favored more diffuse causative features, and their interpretation is probably the most nearly accurate, though at present a less tangible, view of this problem. They based their suggestion on the fundamental work of Needham on the biochemistry of embryology, and stated that the most likely explanation is some interference with the embryologic organization in the lower part of the thorax behind the heart which may affect all structures under development in that area at that time. This theory is not necessarily incompatible with the mechanics of sequestration as put forward by Pryce, but suggests a more basic interpretation.

In this connection it is interesting that these anomalous vessels may be associated with other developmental defects. For instance, they have been described in association with congenital diaphragmatic eventration or hernias,[8,9] and also with pulmonary arteriovenous fistula.[28]

Although it has been thought that hamartomas of the lungs may originate on a basis of sequestration of a small area of the growing pulmonary tree, the view put forward by Jackson in a recent article is of interest. He emphasized that hamartomas are practially unknown during the period of active pulmonary growth, and are commonly found in elderly patients. It may well be that they are a response on the part of pulmonary tissues to some type of hormonal imbalance, just as fibroadenomas of the breast and adenomas of the thyroid, for instance, are thought to be.

INCIDENCE

In our previous review we referred to anomalous arteries from the lower part of the thoracic or upper part of the abdominal aorta to the lower lobes of the lung in 47 cases. In 39 of these cases operation was performed because of intralobar bronchopulmonary sequestration. Analysis of the 47 cases showed that the anomalous artery was on the left in 21 cases, on the right in 11 cases, bilateral in 1 case, and in 14 the side is unknown.

Subsequent literature and our own 5 new cases account for 45 new cases of vascular anomaly. The anomalous vessel was on the right in 19 cases,[7-9,11,16,17,24,26-28] on the left in 17,[6,9,11,16,24,26,28] and the side was not stated in 9 cases.[5,12,13] In 5 cases, however, the anomalous artery was associated with some pathologic process besides intralobar bronchopulmonary sequestration: these consisted of diaphragmatic hernia,[8,9] localized eventration,[8] pulmonary arteriovenous fistula,[27] agenesis of the right lower and middle lobes, cystic disease of the right upper lobe, and absence of the normal hilar vessels on the right.[11] In all 5 of these cases the anomalous artery was on the right. If these 5 cases are omitted from the present group, then the distribution of intralobar bronchopulmonary sequestration reported in this paper is as follows: in 14 cases the condition was on the right, in 17 on the left, and in 9 the side was unknown to us.

Twenty of these 40 patients were males, 10 females, and the sex of 10 was not stated in the reports.

SYMPTOMS AND DIAGNOSIS

The decade of onset of symptoms and the decade of life during which operation was performed are given in the table.

It is again noted in the present cases that intralobar bronchopulmonary sequestration manifests itself clinically and the patients undergo operation, usually before the age of thirty years.

Although the condition is discovered sometimes from routine roentgenograms of the chest made during surveys or annual check-ups, the majority of patients come to surgery because of repeated acute pulmonary episodes associated with intermittent cough, occasional blood-streaked sputum, fever, chills, and the evidence of a

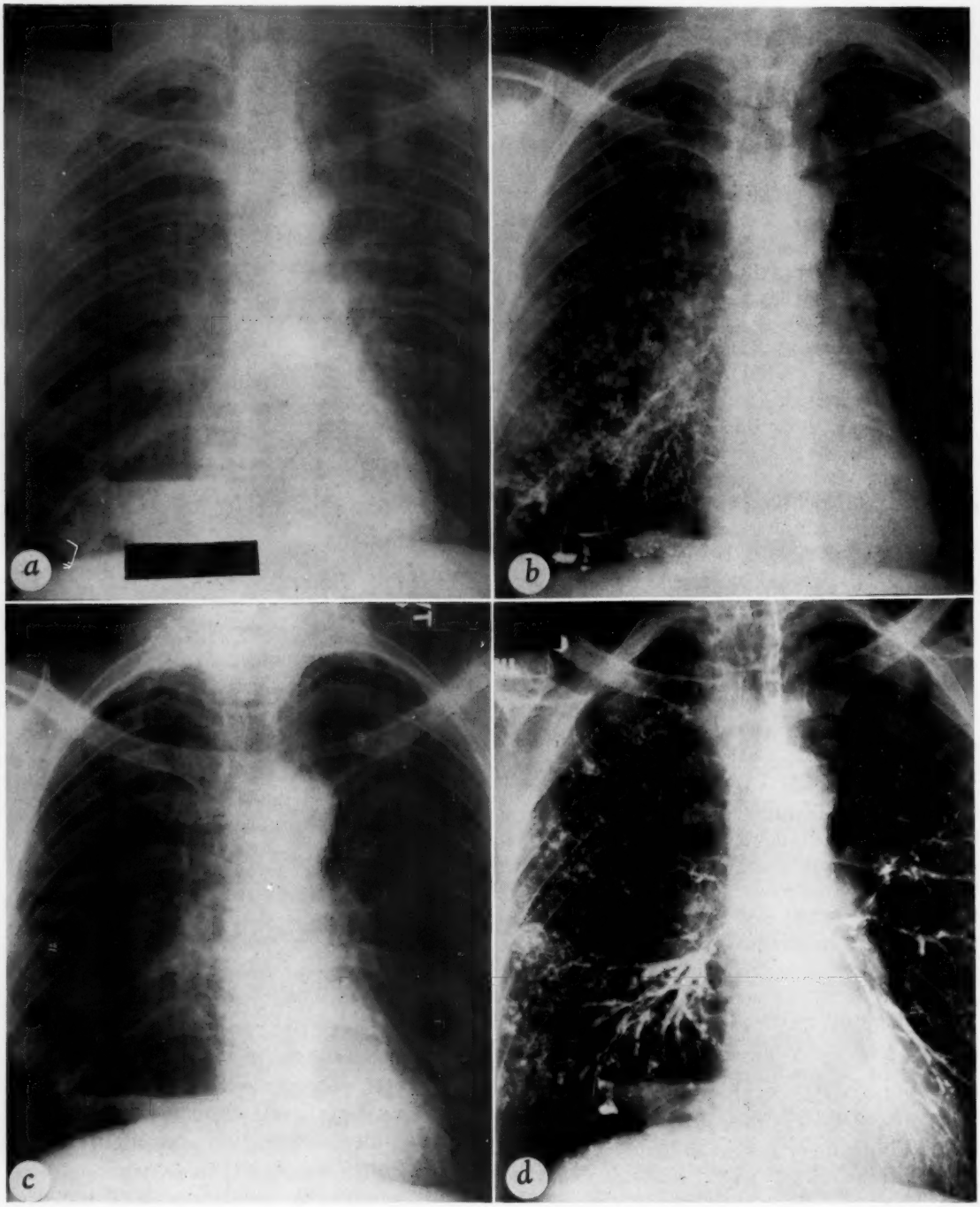

FIG. 2. Case 1(*a*). Posteroanterior roentgenogram taken in 1928. Cavity in right base with air-fluid level. (*b*) Bronchogram made in 1928. There are a few areas of bronchiectasis near the cavity. (*c*) Posteroanterior roentgenogram, taken twenty-three years later in 1951, shows the lesion to be essentially unaltered. (*d*) Bronchogram made in 1951 shows some increase in the bronchiectasis surrounding the cystic lesion. No opaque material has entered the latter in spite of the fact that the air-fluid level indicates that some communication with the bronchial tree must have been present.

AGE AT TIME OF ONSET OF SYMPTOMS AND AT OPERATION

Age in years	Cases*			
	Onset of symptoms		Age at surgery	
	Our previous report	Our present report	Previous	Present
0–9	6	12	3	5
10–19	7	5	7	8
20–29	1	3	5	7
30–39	0	3	2	3
40–49	0	2	2	1
50–59	1	1	1	3
60–69	0	0	0	2
	15	26	20	29

* The discrepancies in figures are due to insufficient data regarding a number of reported cases.

pathologic process in one or other lower pulmonary fields in the roentgenogram.

The roentgenologic findings are strikingly similar in most cases. If at the time a roentgenogram is taken, there is a communication between the bronchial tree and the sequestered region, one or more air-fluid levels willl be seen in the posterobasal area on one side or the other. If no communication exists between the bronchial tree and the sequestered region, the posteroanterior view will show a rounded or oval homogeneous area of increased density ("solid") situated medially in one of the bases. Wyman and Eyler have pointed out that the long axis of the lesion sometimes appears to be directed medially and posteriorly, as if to indicate the possibility of a connection with the lower part of the thoracic or upper part of the abdominal aorta. The lateral view of the thorax for patients who have these "solid" densities in the posteroanterior view, will reveal a surprisingly "misty" and unsubstantial, though well-delineated lesion, and will indicate it to be in the posterobasal segment.

Bronchography practically invariably reveals failure of the opaque material to enter the region of the lesion, whether it is filled with fluid or has an air-fluid level. The adjacent bronchial tree is said to show evidence of underdevelopment in some cases, but too few studies of this sort have been made to allow dogmatic statements. In a few cases there will be evidence of bronchiectasis in the adjacent portions of the lower lobe. Whether this change is related in development to the associated congenital lesion is not known but is rather doubtful.

Bronchoscopy will reveal either an apparently normal bronchial tree or purulent secretions coming from a lower lobe bronchus. The latter finding may indicate an infected cyst, abscess cavity or bronchiectasis.

A number of cases have been encountered in which one or more drainage operations have been performed because of an erroneous diagnosis of lung abscess or empyema following pneumonia. Although the roentgenographic appearance of the lesion in itself is not diagnostic, the finding of a lesion in the characteristic location, usually in a young person who is either symptomless or who gives a history of repeated attacks of pneumonia, makes bronchopulmonary sequestration an outstanding diagnostic probability. Familiarity with the clinical picture and roentgenographic features of bronchopulmonary sequestration has enabled some authors to diagnose the condition before operation.

REPORT OF CASES

Case 1 is of special interest because of the long clinical history, and the early roentgenograms which were still available (Fig. 2).

CASE 1. A man, aged sixty, presented himself in 1951 with the chief complaint of a long history of cough, productive of about a half cupful of yellow sputum per day. Recently he had lost weight and appetite, and had severe malaise, as well as dyspepsia. He had had no night sweats, fever or hemoptysis. Twenty-three years previously the patient had come to the clinic because spells of coughing, productive of large amounts of pus, had occurred for six years. At that time, in 1928, a roentgenogram of the chest had revealed a cavity with fluid level in the right lower lobe, in the posterobasal

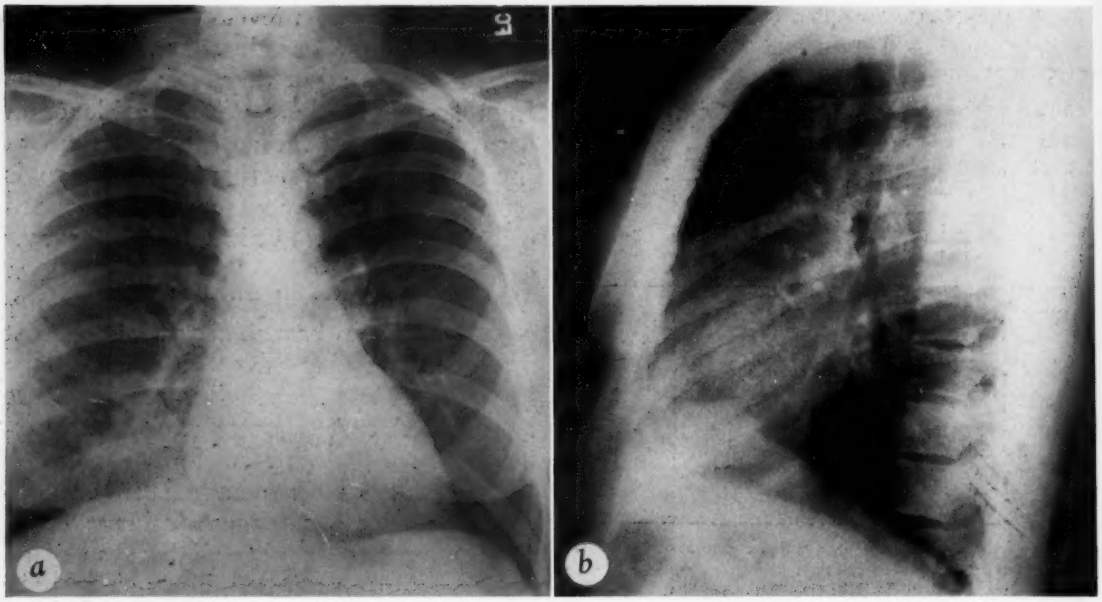

FIG. 3. Case II. The typical location of the cystic lesion in posterobasal segment of the right lower lobe in a woman, who had no symptoms referable to the lungs. The long axis of the lesion appears to be directed medially and inferoposteriorly.[28] (*a*) Posteroanterior view. (*b*) Lateral view.

segment, and bronchograms revealed associated bronchiectasis in this region (Fig. 2*a* and *b*). A great deal of pus was aspirated through the bronchoscope. Phrenicotomy was done and the patient was relieved considerably for a number of years. Roentgenograms and bronchograms were made again during the admission in 1951 (Fig. 2*c* and *d*), and the appearance of the lung was remarkably similar to that twenty-three years previously. Examinations of the sputum for tuberculosis, actinomycosis and other fungi gave negative results. At operation a long band of indurated tissue extended toward the midline from the medial basilar portion of the right lower lobe. This band contained an artery, 0.8 mm. in diameter, apparently coming off the lower part of the thoracic aorta. A cystic structure was felt in the lower lobe, and this part of the lung was very adherent to the diaphragm and lateral thoracic wall. The right lower lobe of the lung was removed. A cyst, 6 cm. in diameter, lined with columnar ciliated epithelium, was present in the posterobasal portion of the lobe. The anomalous artery, which was very sclerotic, ramified around the periphery of the cyst. Some of the surrounding lung tissue was bronchiectatic.

CASE II. A woman, aged thirty-six, who had been in excellent health, came to the clinic because a mass had been found in the chest on routine roentgenographic examination. A roentgenogram made at the clinic showed a well-circumscribed mass in the posteromedial part of the base of the right lung (Fig. 3). Exploratory operation revealed a cyst in the posterior part of the right lower lobe associated with a few adhesions. An anomalous artery from the lower part of the thoracic aorta entered the pulmonary ligament of the right lung. The lower lobe of the right lung was removed, and the patient made an uneventful recovery. The artery was found to ramify in the region of the cyst.

CASE III. A woman, aged twenty-three, came to the clinic because of slight vaginal discharge. She had had some pain in the thoracic portion of the back during the previous winter, and slight blood-streaking of the sputum had occurred a month before admission to the clinic. The routine roentgenogram of the thorax (Fig. 4) showed a dense lesion in the posterobasal segment of the left lower lobe. Bronchoscopy and other examinations gave negative results. At exploratory operation two or three small vessels and one fairly large vessel arose from the thoracic aorta just above the diaphragm and entered the left lobe in the posterobasal region

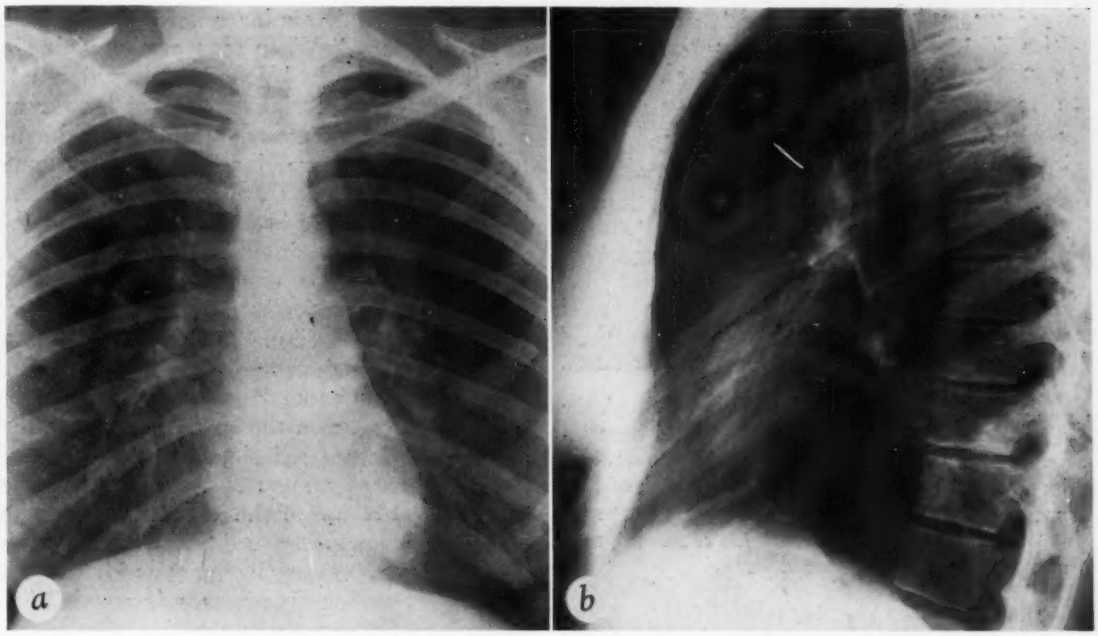

Fig. 4. Case III. Lesion almost identical to that seen in Case II, but on the left side. Patient was a woman, twenty-three years old, who had only minimal symptoms. (*a*) Posteroanterior view. (*b*) Lateral view.

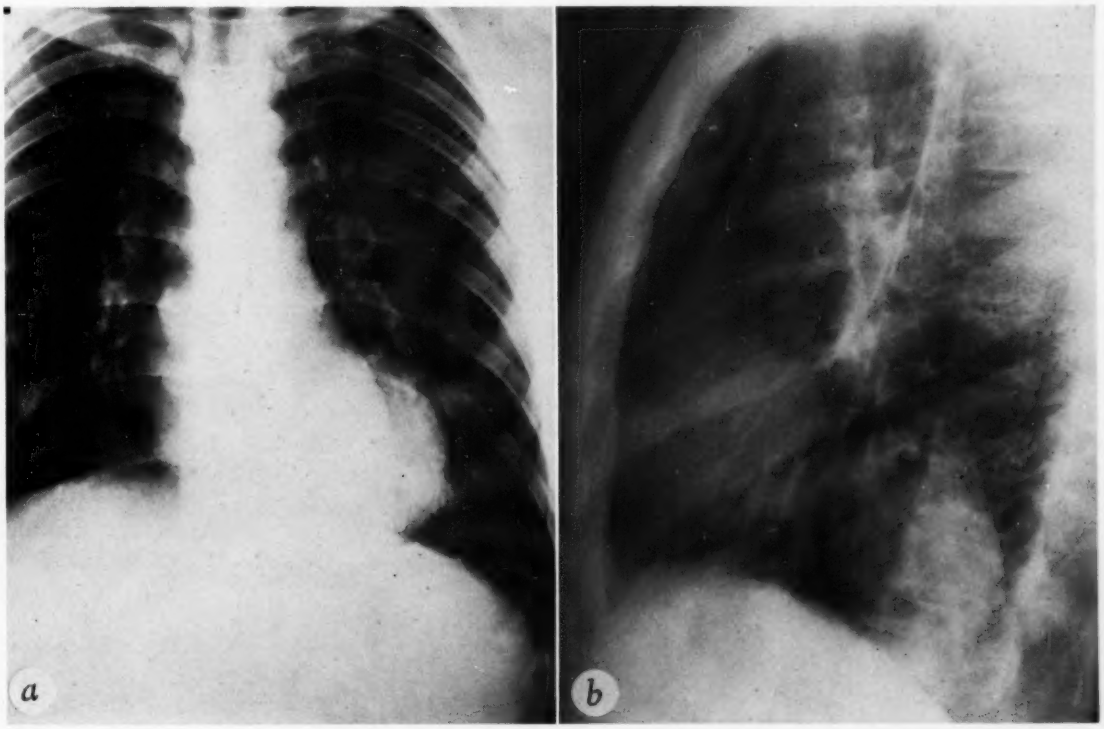

Fig. 5. Case IV. Large cyst in the left posterobasal segment. (*a*) Posteroanterior view. (*b*) Lateral view.

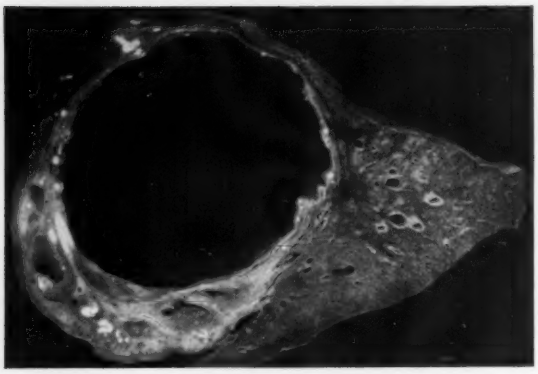

FIG. 6. Case IV. Thick horizontal section through the cystic lesion. The anomalous artery has been injected with barium paste. How the artery confines its distribution to the wall of the cyst should be noted as well as the sharp sequestration of the involved pulmonary tissue from the remaining normal tissue of the left lower lobe.

This portion of the lung was cystic. The lower lobe of the left lung was removed. Pathologic examination revealed a large bronchogenic cyst in the left lower lobe, with branches of the anomalous arteries ramifying in the region of the cyst. In the surrounding lung tissue was a region of lipoid pneumonitis.

CASE IV. A man, aged eighteen, had not been accepted for enlistment into the army on account of an "indeterminate lesion in the base of the left lung." When seen at the clinic six months later, he had no complaints, but admitted that he occasionally cleared his throat and raised a moderate amount of mucoid sputum. On physical examination there was some dullness to percussion at the base of the left lung and diminished breath sounds. Results of other preoperative investigations except for the roentgenograms (Fig. 5) were negative. At operation practically no pleural adhesions were found. A cystic mass, 4 to 5 inches (10.2 to 12.7 cm.) in diameter was felt in the left lower lobe. An anomalous artery, 1.5 cm. in diameter, arose from the aorta, just above the diaphragm. It entered the lowermost part of the pulmonary ligament and proceeded to the posterobasal region of the left lower lobe. The left lower lobe was removed (Fig. 6). The lymph nodes in the pulmonary ligament and hilus were considerably enlarged; microscopic examination showed an inflammatory reaction. Pathologically the cyst in the lower lobe was found to be a bronchogenic cyst.

CASE V. A man, aged fifty-seven, presented himself at the clinic for evaluation of backache. A routine roentgenogram of the thorax revealed an oval mass of homogeneous density in the posterobasal region of the right lower lobe (Fig.

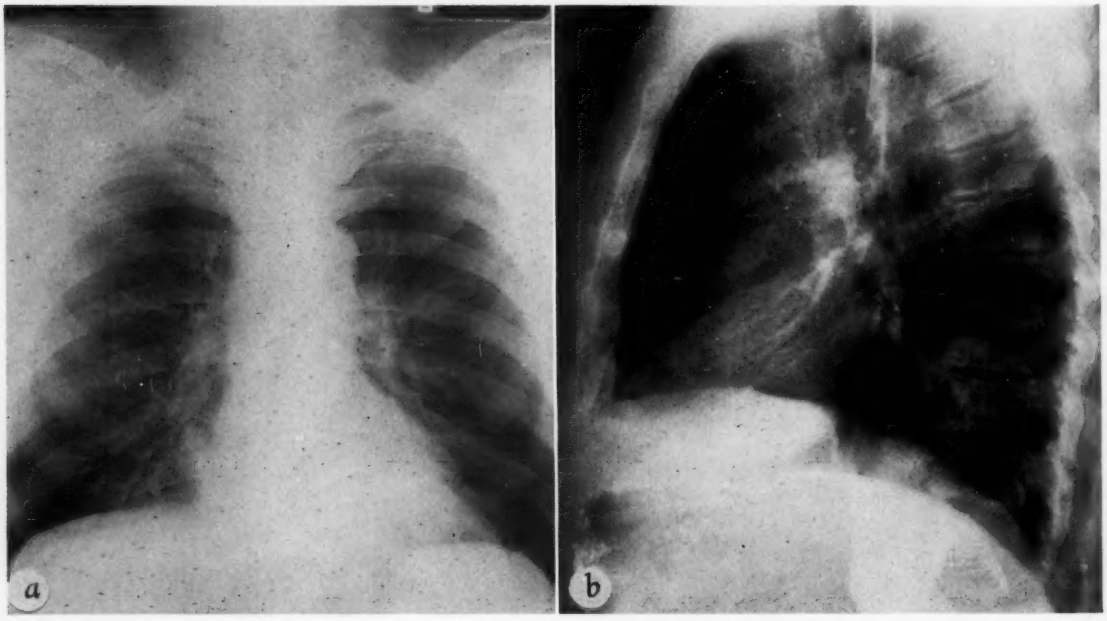

FIG. 7. Case V. (*a*) Oval area of density in right cardiophrenic region. Long axis of lesion is directed downward and medially. (*b*) Lateral view shows lesion in region of posterobasal segment.

7). The long axis of this oval area of density appeared to be directed toward the midline, a feature described by Wyman and Eyler. Bronchoscopy gave negative results. Studies for tuberculosis, fungi and *Brucella*, gave negative results.

At operation, dense adhesions were found in the posterior costophrenic sulcus in the region of the posterobasal segment. A large anomalous artery was found in these adhesions. Considerable difficulty was encountered in ligating this artery, owing to its tendency to retract toward its origin from the lower thoracic aorta after it had been divided.

The left lower lobe was found to contain a large, trabeculated, bronchogenic cyst containing chocolate-colored material. Surrounding it, and in the sequestered region, were many small bronchial structures, but no evidence of alveoli. There was no apparent communication between the cyst and the normal bronchial tree. The anomalous artery was very sclerotic.

PATHOLOGY

The appearance of the gross specimens in these 5 cases was similar to that described by other authors, and in our previously reported cases. The gross abnormality usually falls in one of the three groups of Pryce: (1) a large cyst in the sequestered area, (2) a polycystic mass, or (3) a sequestered mass which contains bronchi that branch parallel to the anomalous artery. In any of these types the bronchial or cystic elements may be completely dissociated from the bronchial tree or there may be a small communication with the bronchial tree, perhaps as a result of infection. Kergin, for example, thought that in 4 out of his 5 cases, the connection of the cystic portion with the bronchial tree was secondary. In a specimen with many cystic portions, some may have small communications with the bronchial tree, whereas others will be totally isolated and filled only with a jelly-like substance, probably inspissated mucus. The cysts are lined with respiratory epithelium. There is no evidence of alveoli in the tissues surrounding the cysts, and no evidence of pigment in the involved pulmonary tissue, as would be expected if any functioning pulmonary tissue had been present. It would appear that the "conducting" component of the involved region (that is, the bronchial component) is abnormally developed and expanded into cystic structures, whereas the "functioning" (alveolar) component is undeveloped. The tissue between the expanded bronchi is largely fibrotic and contains a variable number of inflammatory cells, depending on the amount of infection that had existed. Infection of the sequestered lung tissue may presumably take place by contiguity from an adjacent, temporary lung infection, or by hematogenous spread, as probably occurred in 1 of the cases reported by Pryce.

The anomalous arteries in our 5 cases were confined to the sequestered region. As no veins were found to accompany the anomalous arteries, it is presumed that the venous drainage from the sequestered areas was to the normal pulmonary veins. The anomalous artery usually entered the lung in the region of the lowermost limit of the pulmonary ligament. It is not unusual for large lymph nodes, which may be devoid of pigment, to occur in the region of this accessory hilus. Although these anomalous arteries have been referred to as bronchial type arteries, Pryce has pointed out that they have the histologic appearance of true pulmonary arteries. Not infrequently considerable intimal sclerosis is present, a feature which some authors consider to result from the high pressures in these vessels, but which may also be due to the fact that they are essentially functionless, and that their natural tendency is therefore to deteriorate.

DISCUSSION

Reports of cases of intralobar bronchopulmonary sequestration, which continue to appear in the thoracic surgical literature, tend to confirm the view put forward by Pryce that this condition is a definite clinical, pathologic and embryologic entity. It is also of interest that, among the more recent surgical case reports of anomalous arteries arising from the lower thoracic part or the abdominal aorta or its branches,

there were 2 cases in which the artery was associated with a diaphragmatic hernia, 1 case in which it was associated with agenesis of the lower and middle lobes on the right, and another case in which there was an apparent arteriovenous fistula in the lobe supplied by the anomalous artery. It therefore appears that a number of congenital anomalies in the lower part of the thorax may be associated with the common denominator of the anomalous artery.

Various and divergent findings have been reported concerning whether the smaller branches of the anomalous artery anastomose with the pulmonary artery or with the pulmonary vein. It must be admitted that it is probably exceedingly difficult to determine exactly what communications are made between the finer branches of the anomalous artery and the corresponding branches of the pulmonary arteries or veins or both. By injection methods that we used in our previously reported cases, we were led to believe that the main connections of the anomalous arteries were with the pulmonary arteries, though at what level we could not determine. Other authors have reported similar findings. Thus Tosatti and Gravel, and Cole and associates have demonstrated anastomosis of the anomalous artery with the branches of the pulmonary artery in the adjacent lung field. Cole's group, however, found a free communication between the anomalous artery and the pulmonary vein in 1 case. Such a finding is corroborated by Kergin by injection studies of some of his surgical specimens. Kergin postulated that the extent of this communication may result in a large arteriovenous flow during life and that this may have been the reason why the removal of this anastomosis resulted in an improved exercise tolerance in 1 of his cases.

It is likely that both reported findings are correct. In view of the concept of the origin[10] of the vascular system as an indeterminate network, from which the final arterial and vascular patterns subsequently develop, it would not be surprising to find the anomalous artery communicating with either the pulmonary arteries or pulmonary veins or both, probably at the anteriolar or venular level. If logic may be used in these matters, it seems more reasonable to suspect the anomalous artery to communicate with the pulmonary venous system. But there is good support for the findings of a communication between the anomalous artery and the pulmonary arteries. Thus in Rosenthal's case an anomalous artery which ended blindly in a subpleural position at the base of the lung, communicated with a branch of the pulmonary artery. This blind artery is thought to represent an anomalous artery similar to those we are describing, except that it became separated from the aorta at a late embryologic stage.

Further evidence is the finding by methods of plastic injections of the vesels of removed lungs, that fairly wide communications exist between bronchial arteries and the pulmonary arteries and veins.[25] Although the anomalous arteries in bronchopulmonary sequestration are not histologically similar to bronchial arteries, their origin is undoubtedly similar, and their method of communication with pulmonary arteries and veins may be expected to be similar to that of the normal bronchial arteries.

SUMMARY

Five new cases of intralobar bronchopulmonary sequestration are reported and the recent literature reviewed. The condition is comprised of a cystic lesion in a lower lobe of a lung, intimately associated with a rather large anomalous artery arising directly from the lower thoracic or upper abdominal part of the aorta.

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REFERENCES

1. BENEKE. Quoted by Gruenfeld, G. E., and Gray, S. H. Malformations of the lung. *Arch. Path.*, 1941, *31*, 392–407.
2. BROWN, A. J. The development of the pulmonary vein in the domestic cat. *Anat. Rec.*, 1913, *7*, 299–329.
3. BRUWER, A., CLAGETT, O. T., and MCDONALD, J. R. Anomalous arteries to the lung associated

with congenital pulmonary abnormality. *J. Thoracic Surg.*, 1950, *19*, 957–972.

4. BUELL, C. E., JR. Origin of the pulmonary vessels in the chick. *Contrib. Embryol.*, 1921–1922, *13–14*, 11–26.
5. CARR, D. M. Quoted by Cole, F. H., Alley, F. H., and Jones, R. S.[9]
6. Case Records of the Massachusetts General Hospital, Case 29401: Presentation of case. *New England J. Med.*, 1943, *229*, 591–595.
7. Case Records of the Massachusetts General Hospital. Case 36361: Presentation of case. *New England J. Med.*, 1950, *243*, 383–387.
8. CLAY, R. C., and HANLON, R. C. R. Pneumoperitoneum in the differential diagnosis of diaphragmatic hernia. *J. Thoracic Surg.*, 1951, *21*, 57–70.
9. COLE, F. H., ALLEY, F. H. and JONES, R. S. Aberrant systemic arteries to the lower lung. *Surg., Gynec. & Obst.*, 1951, *93*, 589–596.
10. EVANS, H. M. On the development of the aortae, cardinal and umbilical veins, and the other blood vessels of vertebrate embryos from capillaries. *Anat. Rec.*, 1909, *3*, 498–518.
11. FINDLAY, C. W., JR., and MAIER, H. C. Anomalies of the pulmonary vessels and their surgical significance: With a review of literature. *Surgery*, 1951, *29*, 604–641.
12. HINSON, K. F. W. Personal communication to Tosatti, E., and Gravel, J. A.
13. HUGHES, FELIX. Quoted by Cole, F. H., Alley, F. H., and Jones, R. S.[9]
14. HUNTINGTON, G. S. The morphology of the pulmonary artery in the mammalia. *Anat. Rec.*, 1919, *17*, 165–201.
15. JACKSON, A. V. Five cases of "adenochondroma" of the lung. *Australian & New Zealand J. Surg.*, 1952, *21*, 173–178.
16. KERGIN, F. G. Congenital cystic disease of the lung associated with anomalous arteries. *J. Thoracic Surg.*, 1952, *23*, 55–65.
17. MCDOWELL, C., ROBB, DOUGLAS, HINDS, J. R., and NICK, ROWAN. A case of intralobar sequestration of the lung associated with an abnormal pulmonary artery. *Brit. J. Surg.*, 1951, *39*, 87–91.
18. MESCHAN, ISADORE, and CALHOUN, J. D. Bronchopulmonary hypogenesis; diagnosis in the living. *South. M. J.*, 1950, *43*, 1038–1042.
19. NATUCCI, G. Sopra un caso raro di anomalia delle arterie bronchiali. *Pathologica*, 1939, *31*, 514–520.
20. NEEDHAM, JOSEPH. Biochemistry and Morphogenesis. Cambridge University Press, London, 1942, 787 pp.
21. PRYCE, D. M. Lower accessory pulmonary artery with intralobar sequestration of lung; report of seven cases. *J. Path. & Bact.*, 1946, *58*, 457–467.
22. PRYCE, D. M., SELLORS, T. H., and BLAIR, L. G. Intralobar sequestration of lung associated with an abnormal pulmonary artery. *Brit. J. Surg.*, 1947, *35*, 18–29.
23. ROSENTHAL, S. R. Isolated giant growth of a branch of the pulmonary artery associated with congenital bronchiectasis; report of a case. *Arch. Path.*, 1931, *12*, 387–396.
24. SANTY, P., BERARD, M., GALY, P., and HUU, N. La séquestration pulmonaire kystique avec artère anormale d'origine aortique; a propos de six cas. *J. franç. méd. et chir. thorac.*, 1952, *6*, 101–139.
25. TOBIN, C. E. The bronchial arteries and their connections with other vessels in the human lung. *Surg., Gynec. & Obst.*, 1952, *95*, 741–750.
26. TOSATTI, E., and GRAVEL, J. A. Two cases of bronchogenic cyst associated with anomalous arteries arising from thoracic aorta. *Thorax*, 1951, *6*, 82–88.
27. WATSON, W. L. Pulmonary arteriovenous aneurysm; a new surgical disease. *Surgery*, 1947, *22*, 919–929.
28. WYMAN, S. M., and EYLER, W. R. Anomalous pulmonary artery from the aorta associated with intrapulmonary cysts (intralobar sequestration of lung); its roentgenologic recognition and clinical significance. *Radiology*, 1952, *59*, 658–667.

INTRACEREBRAL ARTERIOVENOUS MALFORMATIONS

THEIR DIAGNOSIS AND ANGIOGRAPHIC DEMONSTRATION*

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ARTERIOVENOUS anomalies are not an uncommon cause of intracerebral disorders and their detection has become an important roentgenographic procedure. In 1928 Cushing and Bailey[10] and also Dandy[11] reported that they were usually found accidentally at operation or at the postmortem examination and that only a few had been diagnosed by clinical means. Cushing considered these cases unsuitable for surgical correction because of their extensive and highly vascular nature. In the twenty years since then, cerebral angiography[13,14] has been perfected, permitting their demonstration and accurate localization, and the neurological surgeons[2,15,18,19,21] have achieved successful methods for their extirpation. These accomplishments have now made arteriovenous malformations of greater clinical concern and require that the radiologist be familiar with their embryologic, pathologic and clinical manifestations.

EMBRYOLOGY

The origin of all vascular anomalies of the brain, with perhaps the exception of the carotid-cavernous fistulas, can be traced to their embryologic development.[10,20,28] The primordial blood-containing channels pass through five stages in the process of development into arteries, veins and capillaries. In the first period, the primordial vascular plexus is established (4–14 mm. embryo). In the second phase, the plexus resolves itself largely into arteries, veins and capillaries (14–18 mm. embryo). In the third period the vascular system is split into three superimposed layers by the development of the dura mater and cranium, resulting in a superficial, dural and pial circulation (18–24 mm. embryo). In the fourth period occurs a series of changes in the arrangement of the vascular trunks (24–50 mm. embryo). During the fifth period, the maturing of the structure of the adult arteries, veins and capillaries takes place.

Thus, a malformation occurring in the third period might well result in a vascular nevus of the face or scalp, varices of the dura, angioma of the pia or brain, or all three simultaneously. Likewise, in the second period, if normal development failed to occur in a certain area, it might be impossible to determine the nature of the resulting vessels, because of their unusual structure and communications.

When one considers the common bed for the development of these vessels and the enormous constructive and destructive changes these primordial vessels must undergo to reach the final pattern, it is a wonder that direct congenital communications between arteries and veins do not occur more frequently. While arteriovenous malformations may occur in any area of the brain, they have a predilection for the rolandic area.[29]

PATHOLOGY

The lesions which are discussed in this report would be considered as true tumors by Cushing and Bailey.[10] Although they are capable of growth and alteration in character, Dandy[11] emphasized their congenital origin and felt that these lesions should not be considered as angiomas. On the basis of existing embryologic and pathologic evidence, it is perhaps best to consider them as arteriovenous malformations.

Cerebral arteriovenous malformations

* Presented at the Fifty-third Annual Meeting, American Roentgen Ray Society, Houston, Texas, Sept. 23–26, 1952.

are almost always associated with angiomas. As such they are capable of alteration in size. They are composed of capillaries, arteries and veins in almost any proportion and always contain some glial tissue between the vessels. They are known to provoke irritative and even pressure symptoms similar to those due to neoplasms. The most reliable method of differentiating between arterial and venous angiomas is from their gross appearance which depends on the predominant color of the blood pulsating through them.

Since the capillary network is missing in arteriovenous anomalies, the arterial blood flows directly into the venous system in one of two ways: (1) by direct communication, although this form is rare in the brain, and (2) by a large tangle of abnormal vessels of varying caliber, most of which are undifferentiated. It is this interposed tangle of blood vessels which forms the volume of most arteriovenous malformations (Fig. 1 and 2*A*, *B*).

By the time the clinical diagnosis has been made, the arteriovenous malformations have usually attained considerable size. The caliber of the arteries proximal to the lesion (feeding arteries) may have enlarged several times that of the normal arteries and the entire arterial tree of the affected hemisphere may be hypertrophied (Fig. 2*A*, *B* and 8*A*, *B*). Even greater dilatation occurs in the emptying veins which may become huge distended venous channels (Fig. 2*C*, *D*).

Histologic examination reveals that the vessels composing the malformations are usually normal in structure without evidence of neoplastic change or inflammatory infiltration. The elastic connective tissue and muscle layers may be normal or thin. The intima or adventitia, or both, may show irregular thinning or thickening. The arteries proximal to the arteriovenous malformations often undergo marked degenerative processes which add to the degree of dilatation. Their walls become thin, the muscular layers atrophy and the elastic tissue diminishes. Deposits of calcification

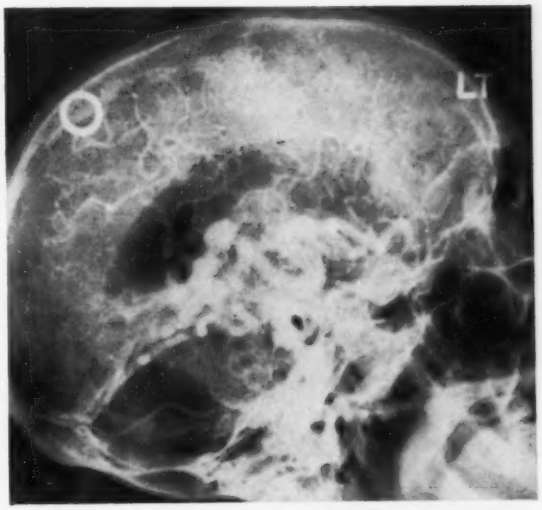

Fig. 1. Extensive tangle of abnormal vessels in a large arteriovenous malformation involving the secondary branches of the right middle cerebral artery and communicating with large dilated venous channels. This illustrates the great volume of tissue that can be occupied by vascular malformations without disturbing the ventricular system.

Case 11. D.A. This man, aged forty-five, had a progressive left hemiparesis for six years, diplopia and memory loss for three years. Ligation of the right internal carotid artery, in contrast to the usual experience, resulted in subjective improvement, clearing of the diplopia and almost complete resolution of the hemiparesis.

can occur in the cerebral tissue adjacent to the walls of the anomalous vessels[2,19] (Fig. 3).

DIAGNOSIS

The diagnosis of arteriovenous malformations is determined from a study of (I) the symptoms and physical findings, and (II) of the cerebral angiograms.

I. *Symptoms and Physical Findings* (Tables I, II and III).

The symptoms and physical findings vary depending upon the communications between the vessels and the pathologic and physiologic changes that occur within and about them and upon the area of the brain that may be affected. On this basis, cerebral arteriovenous malformations can be divided into two groups: (1) the common arteriovenous malformation situated within the brain and associated with an angiomatous mass of vessels, and (2) the carotid

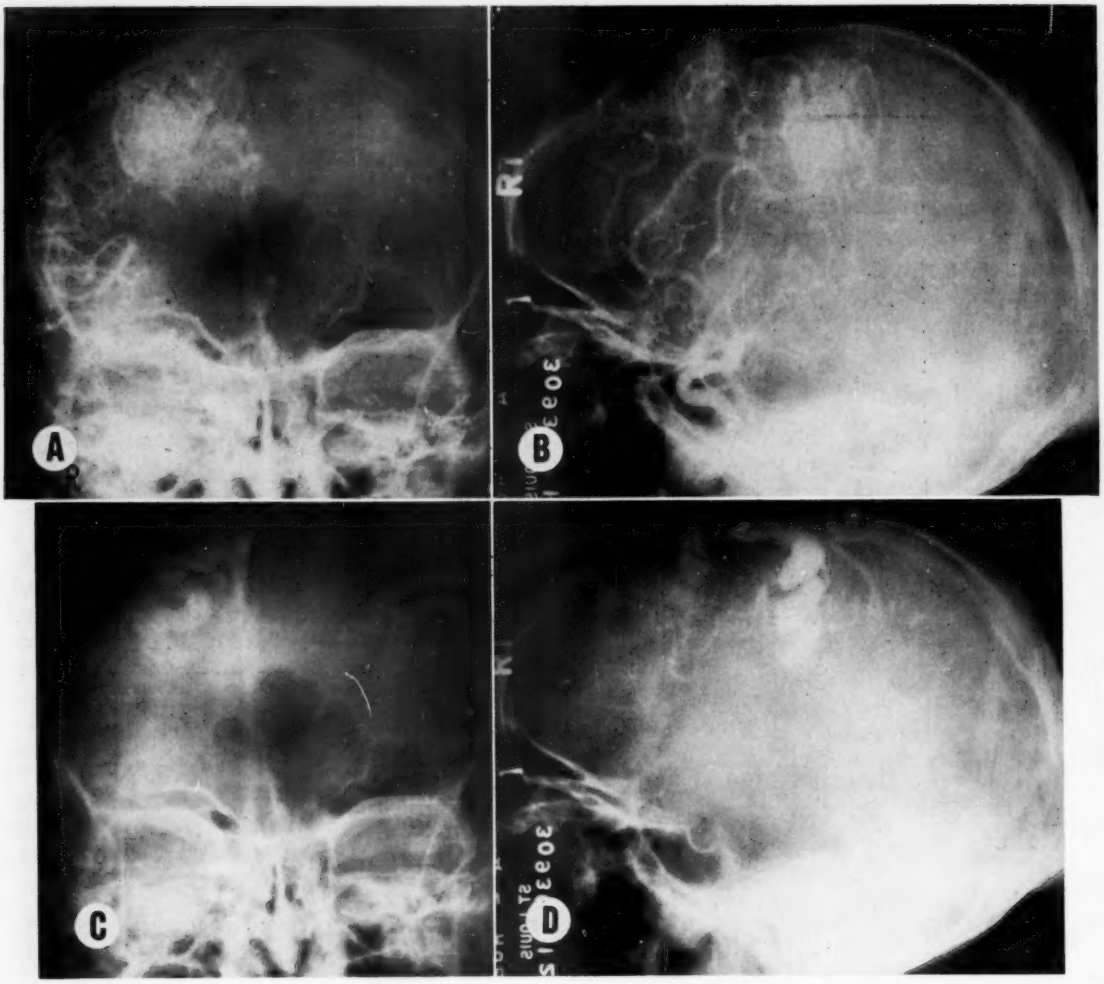

FIG. 2. Large arteriovenous malformation extending from the surface down deep into the brain and limited to the right hemisphere. (*A*) and (*B*) demonstrate that the malformation involves branches of both the anterior and middle cerebral arteries. Note the enlarged caliber of the "feeding" arteries. (*C*) and (*D*) show the huge dilated venous channels that drain into the longitudinal sinus.

Case 21. A. H. A white male, aged thirty-six, with an eight year history of many episodes of nausea, vomiting, stiff neck, convulsions and left hemiparesis due to repeated subarachnoid and intracortical hemorrhages.

cavernous sinus or ophthalmic vein fistulas located at the base of the brain. Of the 22 cases comprising this series, 17 were arterial angiomas with arteriovenous connections and 5 were carotid-cavernous fistulas.

1. Angiomatous arteriovenous malformations: In this group of vascular malformations a relatively large percentage occurred in children. This is probably due to the increasing awareness of pediatricians concerning these disorders. Two of them were under one year of age, 1 was six, 1 was eight, 2 were nine and 1 was thirteen. Eight were in the second and third decades of life and the remaining 2 were forty-five and fifty-one years of age.

The most common symptom was headache. It was present in every case where the patient was old enough to relate his complaints. Generally the headache was sudden in onset and progressive in severity.

The next most frequent symptoms were episodes of unconsciousness and periods of

coma, which occurred in 11 cases. The attacks of unconsciousness could be correlated with subarachnoid or intracortical hemorrhages in 9 of them and were a critical factor in 12 cases. This high percentage of intracranial hemorrhages emphasizes that it occurs sooner or later in most of these patients.

Epileptiform seizures appeared in only 6 patients and are a manifestation of irritation or minor hemorrhages from these vessels which are prone to involve the paracentral convolutions. The subarachnoid or intracortical hemorrhages are obviously the result of a rupture, either spontaneously or secondary to minimal trauma, of these dilated and delicate thin-walled vessels. It is becoming more appreciated that most subcortical hemorrhages, except these due to arteriosclerotic changes, are the result of bleeding from deeply placed arterial malformations.

The mental deterioration, which some authors[19] report as occurring in 50 per cent of these cases, is the result of the markedly abnormal circulatory exchange that occurs in the cerebral tissue of the affected hemisphere and even sometimes of the contralateral hemisphere.

Nausea and vomiting appeared in 8 cases and always occurred with intracranial hemorrhages.

An audible bruit could be heard by the examiner in 5 instances but was apparent to only 1 patient subjectively.

Intracranial calcifications which are considered to be common[19] and characteristic of arteriovenous malformations could be detected in only 4 of our cases (Fig. 3).

Increased intracranial pressure and papilledema occur rarely because the embryologic origin and slow growth of arteriovenous malformations usually permits adequate compensation.

2. Carotid-cavernous fistulas: The symptoms and physical findings in the group of 5 carotid-cavernous sinus or ophthalmic vein fistulas also depend on the number and size of the vessels and the segment of the brain involved and, in addition, on the diameter of the arteriovenous communication. For the most part, the symptoms and signs are pathognomonic in this disorder and consist of a bruit apparent to both the patient and the examiner, pain behind the eye, diplopia, photophobia and a pulsating exophthalmos. These features were present in all cases. Subarachnoid hemorrhage did not occur in them, and convulsions, hemiparesis, nausea, vomiting and dizziness were seldom present. Until recently carotid-cavernous fistulas were considered to develop from trauma to the internal carotid artery at the point where it passes through the cavernous sinus.[21] However, Ruggiero and Castellano[23] have shown that many develop spontaneously, which happened in 3 of our cases.

Fig. 3. This is an example of the characteristic double linear deposits of calcific material in arteriovenous malformations that may occur in the walls of the vessels and in the tissues about them.

In one of them (M.L.), an aneurysm 1.0 cm. in diameter had developed in the internal carotid artery where it lay in the cavernous sinus. It ruptured and a communication developed between the two vessels that

TABLE I

SUMMARIES OF HISTORIES ON 22 CASES OF INTRACRANIAL ARTERIOVENOUS MALFORMATIONS

Case No.	Age	Sex	Race	Diagnosis	Symptoms at Onset	Subarachnoid Hemorrhage*	Bruit	Treatment	Follow-up
1 M.L.	65	F	W	Spontaneous arteriovenous communication between intracranial carotid and cavernous sinus, ophthalmic vein, anterior facial vein and petrosal sinus	Sudden severe right frontal headache, N. and V., diplopia, subjective bruit and pulsating exophthalmos. Paresis of right 2–8th cranial nerves	No	Yes; could be obliterated by carotid pressure	Ligation of right internal carotid artery	Good response initially. Developed propagating thrombus of internal carotid. Heparin was given; pt. died of mediastinal hemorrhage
2 L.S.	40	F	W	Spontaneous arteriovenous communication between internal carotid artery and cavernous sinus and ophthalmic vein	Sudden severe left frontal headaches, proptosis, diplopia, subjective bruit, pulsating exophthalmos	No	Yes	Craniotomy; ligation of abnormal vessels, and ligation of common carotid	Bruit obliterated and pt. well for 6 yr. except for osteo. of flap. Dx of arteriovenous malformation in basilar or vertebral artery. Angiogram on basis of bruit in mastoid areas. Pt. died 7 yr. later of ruptured saccular aneurysms
3 A.O.	33	F	W	Spontaneous arteriovenous communication between ophthalmic vein and angioma just distal to carotid artery siphon. Pt. also had long history of multiple hemangiomas of nose and mouth	Developed gradual rt. hemiplegia at age 18. Sudden onset of pulsating exophthalmos and subjective bruit 2 weeks before admission to hospital	No	Yes	Ligation of common carotid in neck	Bruit obliterated. Developed thrombus of ophthalmic vein with blindness resolved spontaneously and completely. Pt. continued to have severe epistaxis relieved somewhat by coagulation of nasal hemangiomas
4 L.C.	25	F	W	Traumatic arteriovenous communication between left internal carotid artery and cavernous sinus, vein of Galen and other cerebral veins	Onset of left pulsating exophthalmos, diplopia and pain 10 days after light trauma to left temporal area	No	Yes	Triple ligation of carotid arteries in the neck	Bruit partially obliterated. Exophthalmos improved
5 J.S.	29	M	C	Arteriovenous communication between right internal carotid artery and rt. cavernous sinus and superior petrosal sinus, both ophthalmic veins and rt. jugular vein	Developed pulsating exophthalmos, pain, diplopia immediately after light blow on neck with a cane	No	Yes	Triple ligation of right carotid arteries in the neck	Bruit diminished; headache cleared and eye returned to normal
6 M.F.	9	M	W	Sturge-Weber's syndrome with port wine facial nevus and left parietal angioma with calcification about it	Rt. sided convulsions and hemiplegia at 5 mo. Headache and tonic convulsions and petit mal, all progressively severe to age 9 yr.	No	No	Roentgen treatment, 1,200 r (air) to each of 4 10×10 cm. ports over 2 week period	Much improved mentally and physically but still has occasional grand mal seizures
7 P.D.	37	F	W	Small arterial angioma (2 cm. in diameter) rt. parietal lobe	Sudden severe headache, occipital pain, stiff neck, prostration for 24 hr.	Yes	No	None	None
8 J.C.	26	M	W	Angioma at base of left frontal lobe above orbital plate	Sudden severe headache, occipital pain, N. and V., unconsciousness, followed by gradual onset of blindness in left eye in one week	Yes	No	Cranitomy with evacuation of organizing hematoma about angioma. Ligation of common carotid	No further symptoms in 2 yr. Continues blind in left eye
9 E.B.	51	M	W	Angioma of left parietal lobe; also saccular aneurysm at origin of right anterior cerebral artery	Left frontal headache with diminution of vision 1 week. Generalized convulsion beginning on right with incontinence and apnea	Yes	No	Craniotomy with clipping and obliteration of aneurysm, evacuation of blood clot and resection of rt. frontal lobe	Pt. died one day postop. Autopsy revealed another saccular aneurysm of rt. anterior cerebral artery at junction of ant. communication art. Angioma with rupture 1.5 cm. below surface left parietal
10 J.E.	8	F	W	Arteriovenous malformation posterior to sella at base of brain arising from left middle cerebral artery	Sudden headache N. and V., stiff neck, photophobia followed by unconsciousness	Yes	Yes	Surgery felt to be contraindicated. Roentgen treatment advised but refused	Pt. recovered spontaneously. Still well 1 year later. Bruit still present
11 D.A.	45	M	W	Extensive arteriovenous malformation in floor and central portion rt. hemisphere, involving secondary branches rt. middle cerebral artery	Progressive left hemiparesis 6 yr. Diplopia 3 yr. Blurred vision and memory loss	No	No	Ligation of right internal carotid	Marked improvement subjectively. Diplopia cleared. Hemiparesis cleared except for left hand

TABLE I—(*continued*)

Case No.	Age	Sex	Race	Diagnosis	Symptoms at Onset	Subarachnoid Hemorrhage*	Bruit	Treatment	Follow-up
12 S.N.	11 mo.	F	W	Arteriovenous malformation involving anterior and middle cerebral artery branches and longitudinal sinus	Baby would pound head and cry and hold temples. Mother heard bruit	No	Yes	Roentgen treatment	None
13 J.F.	23	M	W	Arteriovenous malformation arising from posterior branches left anterior cerebral artery in parietal area	Sudden exacerbation of chronic headache and vomiting 8 times in 4 yr. No convulsions or unconsciousness	Yes	No	Roentgen treatment, 1,500 r (air) to each parietal area in 2 weeks	Followed 2 yr. without recurrence except for one minor episode
14 M.M.	9	M	W	Extensive arteriovenous malformation involving left ant. cerebral artery and longitudinal sinus. Porencephaly and intracortical hematoma secondary to rupture of vessels	Sudden onset of severe frontal headache, vomiting, convulsions with fecal and urinary incontinence and coma	Yes	No	Surgical extirpation of entire lesion by left frontal lobectomy	4 yr. follow-up shows pt. completely well. No seizures now. Doing well in school
15 R.C.	30	M	W	Arteriorvenous malformation in parieto-occipital area involving vessels of dura, middle cerebral, artery and sigmoid sinus	Severe headaches; episodes of loss of consciousness; jacksonian sensory epilepsy	No	Yes	1. Ligation of internal carotid artery 2. Attempted surgical extirpation of malformation	1. Minor improvement 2. Pt. died 2 days postop. No autopsy
16 T.W.	10 mo.	M	W	Lymphangioma of scalp. Arteriovenous malformation involving rt. mastoid area in middle cerebral artery, external circulation and transverse sinus	Hydrocephalus and slow physical development	No	Yes	1. Ligation of common carotid 2. Attempted cauterization and ligation of abnormal communicating vessels	1. Cessation of bruit. 2. Pt. died 12 hrs. postop. Autopsy showed a large venous component compressing cerebellum and obstructive hydrocephalus. Longitudinal and lateral sinuses involved
17 F.M.	28	M	W	Multiple hemangiomas of spinal cord dura, arteriovenous malformation involving rt. anterior communicating artery, middle meningeal artery and large venous lakes in occipital region	Sudden severe headache, back and leg pain. Loss of consciousness, left homonymous hemianopsia	No	Yes	1. Triple ligation of carotid arteries on right. 2. Roentgen treatment	Headache diminished and back pain slightly improved. Bruit and other symptoms unchanged
18 R.K.	22	M	W	Large arteriovenous malformation fed by supracallosal artery and draining into vein of Galen. Choroid plexus left lateral ventricle also involved	Sudden severe dizziness. N. and V., scotomas, photophobia and stiff neck. Previous history of many episodes of headache and stiff neck for 10 yr.	No	No	Surgical extirpation of lesion	Died 10 hr. postop. of cerebral edema and thrombosis. No autopsy
19 P.C.	21	F	W	Small arteriovenous malformation frontoparietal area fed by middle cerebral artery branches and drainage into vein of Labbé	Dull headache with sudden onset of N. and V. aphasia, hemiparesis and coma	No	No	None	No further symptoms in 2 yr. No residual signs
20 K.H.	13	M	W	Extensive arteriovenous malformation involving branches of middle cerebral artery in region of angular gyrus draining into petrosal sinus. Subarachnoid and intracortical hemorrhage	Headaches 3 mo. followed by sudden severe pain in left eye and coma	Yes	No	Surgical extirpation of entire lesion	No further symptoms
21 A.H.	36	M	W	Large arteriovenous malformation involving anterior and middle cerebral artery branches and longitudinal sinus	8 yr. history of episodes of N. and V., stiff neck, convulsions left hemiparesis	Yes	No	None; pt. deferred operation	None
22 C.E.	6	F	W	Large venous angioma fed by three arteries from midline and from sylvian fissure and draining into both longitudinal sinuses involving left parietal lobe from falx to sylvian fissure	Convulsions from age of 4 mo.; mental retardation, rt. sided weakness and ataxia	No	No	Coagulation of all major vessels forming the anomaly	Pt. improved slowly after operation with some increase in ability to talk. Continued to have occasional mild convulsions

* "Subarachnoid hemorrhage" in this table means at the time of hospitalization.

TABLE II

PHYSICAL FINDINGS

	Bruit	Intracranial Hemorrhage	Total or Partial Hemiparesis	Intracranial Calcification	Other Vascular Anomalies	Hydrocephalus	Pulsating Exophthalmos
Carotid Artery and Cavernous Sinus or Ophthalmic Vein Fistulas (5 cases)	5	0	1	0	3	0	5
Other Arteriovenous Malformations (17 cases)	5	12	7	4	3	1	0

measured 3.0 mm. in diameter and was covered by endothelium (Fig. 4). In another (L.S.) multiple large saccular aneurysms were found at the base of the brain and the rupture of one of them was the eventual cause of death. It is reasonable to assume that a rupture of a similar aneurysm was the cause of the spontaneous carotid-cavernous sinus communication. The third case (A.O.) had a clearly demonstrated arterial angioma at the base of the brain and the rupture of it created the carotid-ophthalmic vein fistula (Fig. 5). One of the 2 other cases (J.S.) revealed a communication between the right carotid artery and both ophthalmic veins (Fig. 6).

II. *Cerebral Angiography.*

Cerebral angiography is indispensable for the comprehensive visualization of the location, size, extent, arrangement and connections. The technique of cerebral angiography is now performed with only minor risk. Satisfactory examinations can be made with conventional equipment employing a standard Potter-Bucky grid, with fast automatic cassette changers, or with roll film cassettes. The important factor is to choose one particular method and to perfect it, so that the timing of the roentgen exposures can be made at the proper moments.

Most of our examinations were made on a biplane angiographic unit designed by Scott and associates[25,26] utilizing two roll film cassettes with thyrotron timers for regulating the frequency, the length of a series of exposures and the time interval between each series of exposures (Fig. 7). The roll film cassettes are equipped with fast self-cocking Potter-Bucky grids and with special cones that limit the roentgen-

TABLE III

HISTORY AND SYMPTOMATOLOGY

	Headaches	Episodes of Unconsciousness	Subjective Bruit	Photophobia	Nausea and Vomiting	Diplopia	Total or Partial Blindness	Convulsions	Pulsating Exophthalmos	Dizziness	Aphasia	Irritating Trauma	Memory Loss
Carotid Artery and Cavernous Sinus or Ophthalmic Vein Fistulas (5 cases)	4	0	5	5	2	5	1	0	5	0	0	2	0
Other Arteriovenous Malformations (17 cases)	15	11	1	2	8	1	5	6	0	3	3	0	1

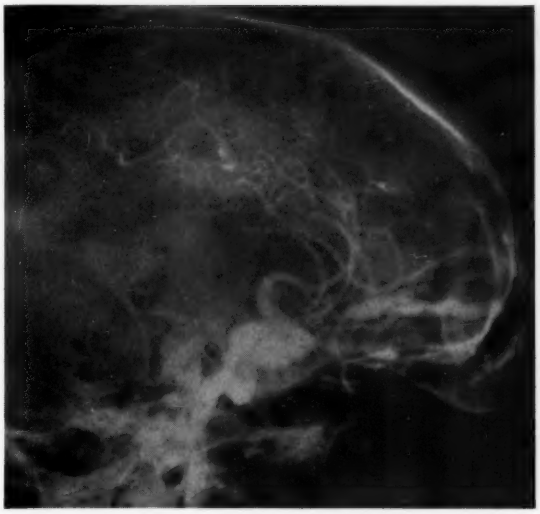

Fig. 4. Angiogram of a carotid-cavernous sinus fistula that resulted from a spontaneous arteriovenous communication between a large aneurysm of the internal carotid artery and the cavernous sinus, ophthalmic vein, anterior facial vein and petrosal sinus.

Case 1. M.L. This woman, aged sixty-five, had a sudden severe right frontal headache accompanied by nausea, vomiting, diplopia, subjective bruit, pulsating exophthalmos, and paresis of right second to eighth cranial nerves. The internal carotid artery was ligated with an excellent initial response. Unfortunately, a propagating thrombus developed and the patient died from a hemorrhage into the mediastinum following heparin therapy.

ray beams to the size of the film frame. Exposures for both the horizontal and vertical units are made alternately usually at 1/20 of a second and at the rate of two per second.

Biplane angiographic units afford the advantage of obtaining lateral and anteroposterior views after a single injection of contrast medium and thus eliminate the hazard of multiple injections. The continuous series of exposures provides the nicety of observing the phases of arterial filling and venous drainage of the cerebral circulation, as well as allowing the use of smaller amounts of the contrast medium. Recently we have been using 7–10 cc. of urokon sodium 30 per cent with satisfactory results. Most of the injections were made by the percutaneous route into the carotid artery.

Both lateral and anteroposterior views should always be made, not only for the accurate localization of the arteriovenous anomaly, but also to be certain that another does not exist in the opposite hemisphere (Fig. 8*A*, *B* and 9*A*, *B*). Frequently it is advisable to make bilateral injections for this purpose and also to determine whether or not afferent arterial or efferent venous components cross the midline. In the presence of enlarged vessels or angiomas in the scalp, the external carotid artery should also be filled, as its branches not infrequently communicate through the skull with those forming an intracranial vascular malformation (Fig. 10*A*, *B* and 11*A*, *B*).

Cerebral angiography has been used in the Scandinavian clinics postoperatively to determine the completeness of removal of the malformation and the effects of the operation on the circulation of the brain.

Fig. 5. Spontaneous arteriovenous communication between an angiomatous maze of vessels and the ophthalmic vein.

Case 3. A.O. A white female, aged thirty-three, who had had a slowly developing right hemiplegia since the age of eighteen. Two weeks before admission to the hospital, she developed a sudden pulsating exophthalmos and subjective bruit. A ligation of the right common carotid artery produced complete relief. This patient had multiple hemangiomas of the nasal and oral mucous membranes which should make one suspect the presence of a similar vascular disorder within the brain.

FIG. 6. Posteroanterior view of a carotid-cavernous fistula with communication between the right internal carotid artery and both ophthalmic veins, the right cavernous sinus, right superior petrosal sinus, and right jugular vein.

Case 5. J.S. This twenty-nine year old colored man developed a pulsating painful exophthalmus and diplopia immediately after receiving a light blow on the neck with a cane. A triple ligation of the right carotid arteries corrected these complaints.

Norlén,[18] Wickbom,[33] and Bunner[8] report that the dilated afferent arteries and efferent veins return to a normal caliber in three or four weeks after the complete removal of an arteriovenous malformation.

PROGNOSIS AND TREATMENT

The ultimate prognosis of these patients is grave, as the duration of life is most uncertain. Usually these patients must endure years of epileptic seizures, severe headaches, recurrent subarachnoid and intracortical hemorrhages, and probably hemiplegia.

This explains why the neurological surgeons[2,3,18,19,21,24,29] now urge complete surgical extirpation of all accessible arteriovenous malformations. The Norwegian neurological surgeons report that very little, if any, benefit follows ligation of accessible arteries or of the carotid artery and many times may result in greater harm. The neurological surgeons in our group emphasize that each patient must be evaluated individually and that the criteria for or against operative procedures will depend on: (1) the severity of the symptoms; (2) the location of the vascular anomaly within the brain; (3) the angiographic picture of the extent, depth, and distribution of the feeding and draining channels of the lesion, and (4) a careful estimate of the disability that would result from extirpation. (Fig. 12*A*, *B*). For example, a patient who has only an occasional convulsion and who has never had a serious hemorrhage is probably better treated with anticonvulsant drugs, because the surgical effort may result in a hemiplegia and the convulsions may not be entirely controlled. On the other hand, the patient who has frequent episodes of intracerebral bleeding has such a grave prognosis that serious surgical measures are justified, even though they may result in

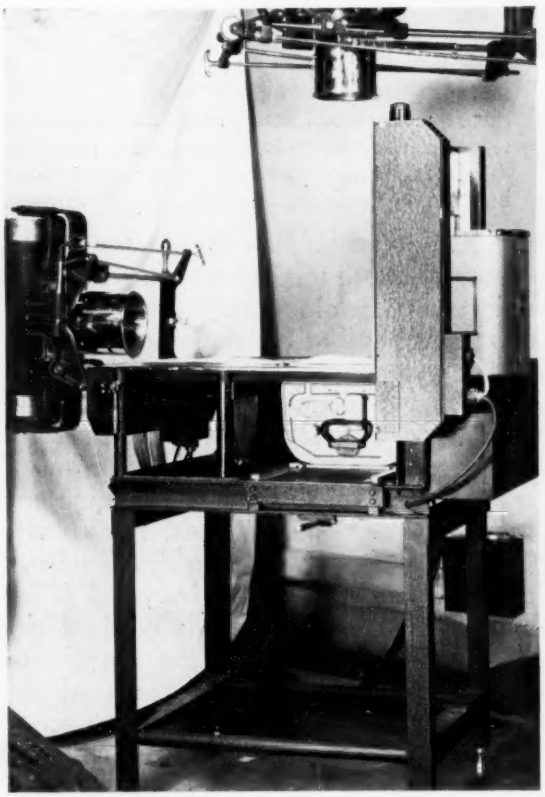

FIG. 7. Equipment for biplane cerebral angiography with two roll film cassettes mounted at right angles and synchronized with self-cocking grids.

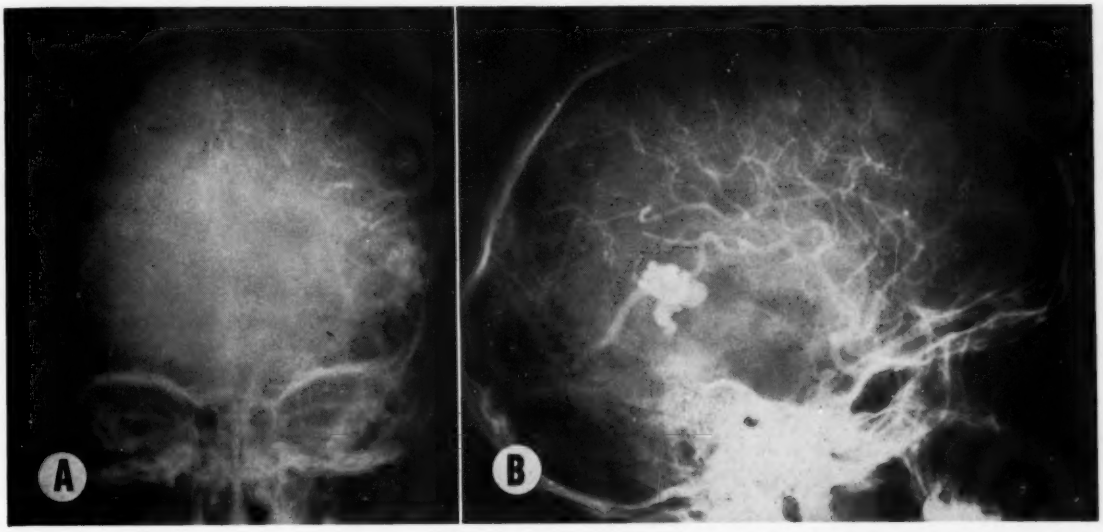

Fig. 8. (*A*) and (*B*). Moderately large arteriovenous aneurysm lying close to the surface in the region of the angular gyrus. This vascular malformation is fed by the left middle cerebral artery and drains into the petrosal sinus. It is the size and location best suited for surgical extirpation which was done in this case with complete relief of symptoms.

Case 20. K. H. A thirteen year old boy who had complained of headaches for three months. These were followed by sudden severe pain in the left eye ending in a coma obviously due to subarachnoid and intracortical hemorrhage from the angiomatous mass of vessels.

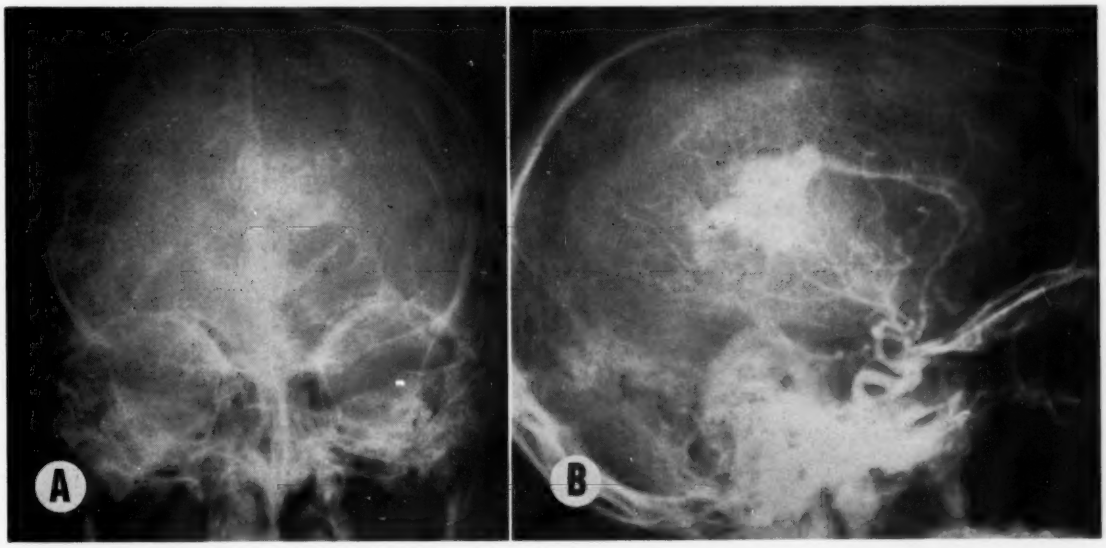

Fig. 9. (*A*) and (*B*). Large arteriovenous malformation situated deep in the left hemisphere fed by the supracallosal artery and drained by the vein of Galen. The size and location of this vascular anomaly, which extended into the lateral ventricular and choroid plexus, made the attempt at surgical extirpation extremely difficult. The history of repeated intracortical hemorrhages justified the risk of surgical removal.

Case 18. R. K. A twenty-two year old man who had experienced repeated episodes of headaches, stiff neck and signs of intracortical hemorrhages over a period of ten years. Just prior to hospitalization he suddenly became dizzy, nauseated, vomited and developed a photophobia and a stiff neck from another hemorrhage.

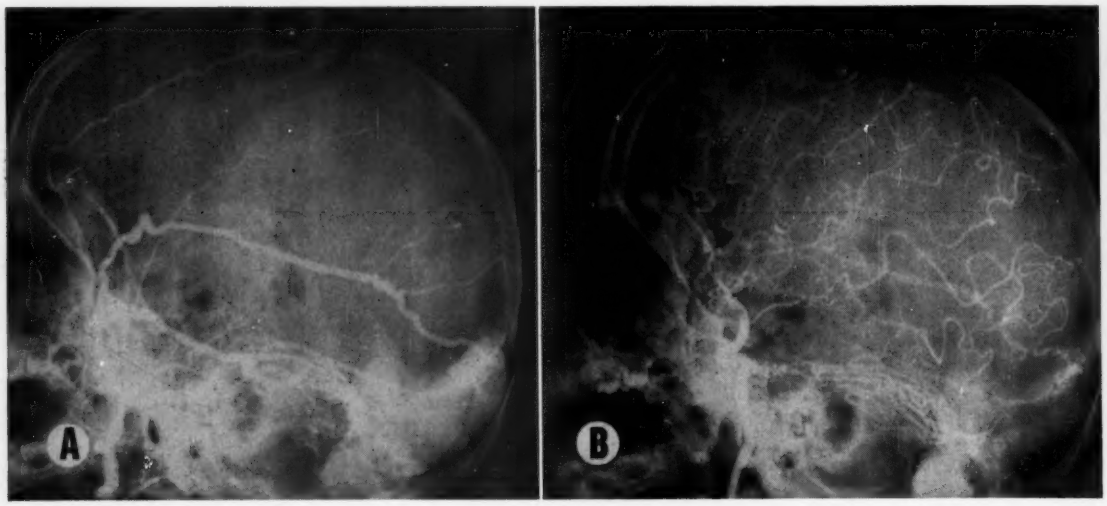

FIG. 10. Huge venous lake involving the longitudinal and lateral sinuses resulting in compression of the cerebellum with obstructive hydrocephalus. (*A*) Angiogram after injection of the external carotid reveals the large feeding arteries that communicate with the intracranial arteriovenous malformation. (*B*) Angiogram after the injection of the internal carotid artery reveals that intracranial branches of it also communicate with the vascular malformation.

Case 16. T. W. A ten month old male with lymphangioma of the scalp and an obvious hydrocephalus. Ligation of the common carotid artery was done first and followed later by a craniotomy with attempted cauterization and ligation of the abnormal communicating vessels.

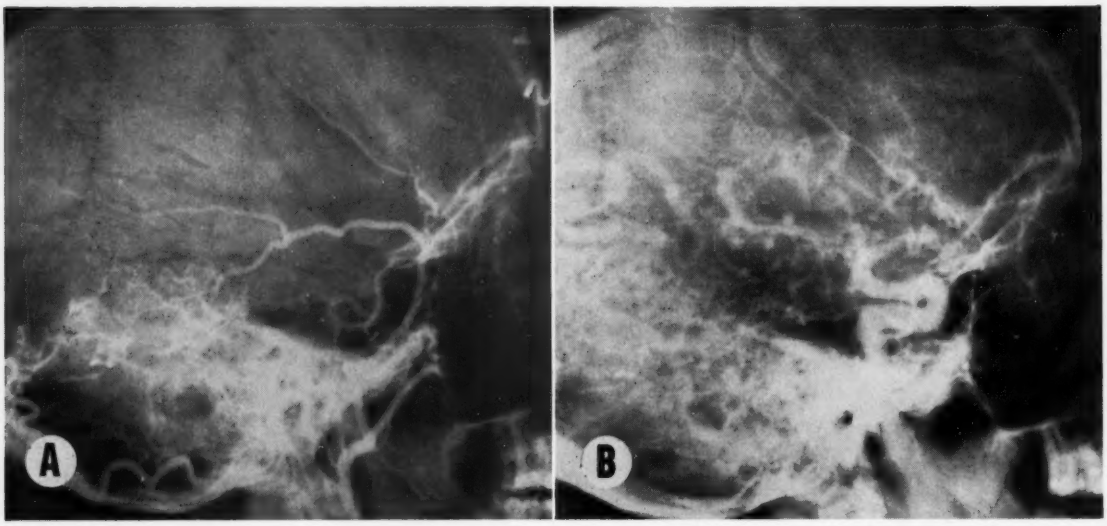

FIG. 11. Frequently intracranial vascular malformations communicate with branches of the external carotid artery as shown in (*A*) which emphasizes the complex circulation of these disorders and the necessity for their complete visualization prior to surgical intervention. (*B*) Angiogram after injection of internal carotid artery demonstrates the great extent of the vascular malformation which was obviously too large for surgical removal.

Case 17. F. M. A twenty-eight year old man who experienced a sudden severe headache with back and leg pains accompanied by a loss of consciousness and a left homonymous hemianopsia. He was treated by a triple ligation of the carotid arteries on the right and deep roentgen therapy, with slight improvement.

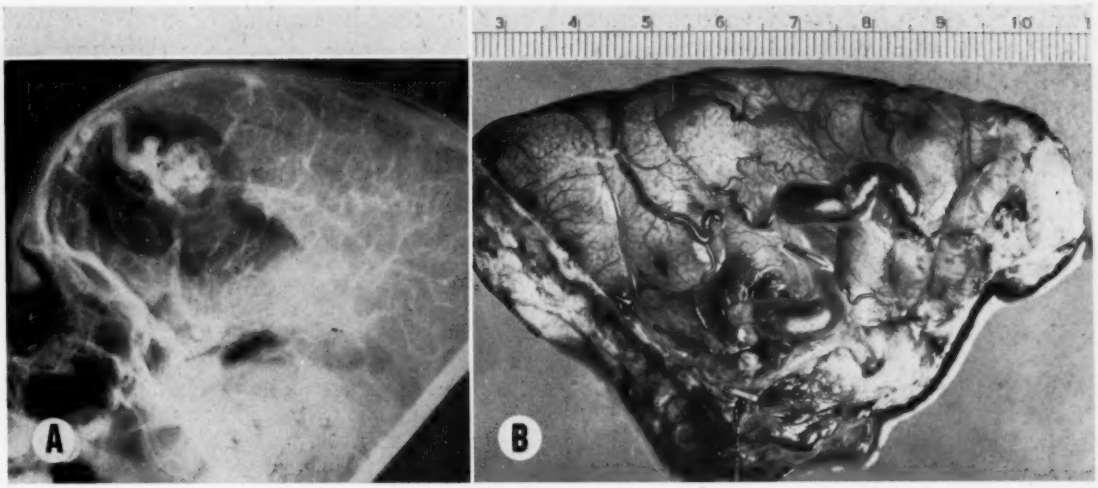

Fig. 12. Moderately large arteriovenous malformation within a porencephalic cavity which is outlined by air after pneumoventriculography.* (*A*) The malformation involves the anterior cerebral artery and longitudinal sinus. (*B*) Photograph of major portion of anterior lobe that was successfully excised. Note the large number of dilated vessels and the extensive area that they involve.

Case 14. M. M. A nine year old boy who developed severe frontal headaches accompanied by vomiting, convulsions, fecal and urinary incontinence and coma. The entire malformation was successfully removed by a left frontal lobectomy with complete recovery.

* (Reproduced by permission from Schwartz, H. G. Subarachnoid hemorrhage and intracranial aneurysm. *Postgrad. Med.*, 1948, *4*, 307–314.)

permanent disabling neurological damage.

Occasionally the lesion may be extensive, yet superficial, and if a neurologically important area is involved, it may be preferable to coagulate it rather than to excise it as was done in Case 22 (C.E.).

When the lesion is in a vital area and surgical removal is impossible, radiation therapy should be considered. Most radiation therapists consider it an uncertain therapeutic measure and point out that radiation in quantities sufficient to obliterate the abnormal vessels would also cause irreparable damage to the normal brain substance.[2,4,19] Consequently radiation therapy is not recommended unless the patient refuses operation and the treatment can be directed to a localized area.

Carotid-cavernous fistulas usually respond to simple ligation of the carotid artery in the neck. This treatment is highly effective. Failures occasionally result due to persistent collateral circulation from the other side of the circle of Willis or from retrograde flow through the ophthalmic artery.

CONCLUSIONS

(1) Intracerebral arteriovenous malformations are a more frequent cause of intracranial disorders than was formerly believed. Their recognition has assumed greater importance as advances in neurological surgery make many of them amenable to extirpation.

(2) The origin of all vascular anomalies in the brain, with perhaps the exception of some of the carotid-cavernous sinus fistulas, can be traced to abnormalities in their embryologic development.

(3) Intracerebral arteriovenous malformations are capable of autonomous and expansile growth.

(4) The history and symptomatology of these arteriovenous malformations depend on their location and extent within the brain and whether they result in episodes of subarachnoid or intracerebral hemorrhage.

(5) Intracerebral arteriovenous malformations can be separated on the basis of their history, symptomatology and physical findings into two groups: (1) the arte-

rial angiomas with arteriovenous connections, and (2) the carotid-cavernous sinus or ophthalmic vein fistulas.

(6) The physical signs and symptoms of vascular malformations of the brain frequently make their appearance early in life, because of the congenital nature of the disorder. Consequently, physicians should keep this possibility in mind when examining children with convulsive seizures or epileptic manifestations.

(7) Cerebral angiography is indispensable for the comprehensive understanding of the location, size, extent, arrangement and vascular connections of intracerebral arteriovenous malformations. Cerebral angiography can be satisfactorily performed with conventional roentgenographic equipment and involves only a minor risk. The advantages offered by biplane angiography with roll film cassettes are desirable.

(8) Treatment of arteriovenous malformations is surgical extirpation whenever feasible. The criteria for surgical intervention are based on the comprehensive angiographic visualization of the vascular malformation, on its location within the brain and on a careful evaluation of the neurological damage that may result from the surgical effort as compared to the severity of the symptoms and the ultimate prognosis.

(9) In the large group of angiomas with arteriovenous communications, the results from ligation of the main feeding arteries or of the internal carotid artery have been disappointing. If surgical measures are not advisable for the patients in this group, radiation therapy can be used if the lesion is superficial and localized to a small area, although the results are usually indefinite.

In the group with carotid-cavernous sinus fistulas, ligation of the internal carotid artery is an effective measure.

(10) The total size of the vascular anomaly is relatively unimportant, since even a small one, by virtue of its location and tendency to hemorrhage, can be a devastating experience. The important factor is that they be found as their diagnosis can now be readily established and operative techniques are available for the successful extirpation of many of them.

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REFERENCES

1. Adams, H. D. Congenital arteriovenous and cirsoid aneurysms. *Surg., Gynec. & Obst.*, 1951, *92*, 693–697.
2. Bancroft, F. W., and Pilcher, C., Editors. Vascular anomalies of the brain. In: Surgical Treatment of the Nervous System. J. B. Lippincott Company, Philadelphia, 1946, pp. 239–246.
3. Bassett, R. C. Symposium; intracranial vascular abnormalities; surgical experiences with arteriovenous anomalies of brain. *J. Neurosurg.*, 1951, *8*, 59–74.
4. Bassett, R. C., and Gass, H. H. Ligation of internal carotid artery for aneurysmal lesions of circle of Willis. *J.A.M.A.*, 1951, *147*, 842–846.
5. Borst, M. Echte Geschwulste. In: Aschoff, L., Pathologische Anatomie; ein Lehrbuch für Studierende und Aerzte, bearb. Jena, G. Fischer, 1913.
6. Bosher, L. H., Jr., Smith, D. E., Lemmer, R. A., and Bigger, I. A. Experimental arteriovenous fistula: histologic changes in small collateral arteries. *Surgery*, 1951, *29*, 560–567.
7. Broman, T., Forssman, E., and Olsson, O. Further experimental investigations of injuries from contrast media in cerebral angiography; summation of various injurious factors. *Acta radiol.*, 1950, *34*, 135–143.
8. Bunner, R. Angiographic studies of cerebral vessels in arteriovenous aneurysms. *Acta radiol.*, 1949, *31*, 233–239.
9. Curry, R. W., and Culbreth, G. G. Normal cerebral angiogram. Am. J. Roentgenol. & Rad. Therapy, 1951, *65*, 345–373.
10. Cushing, H., and Bailey, P. Tumors Arising from the Blood Vessels of the Brain; Angiomatous Malformations and Hemangioblastomas. Charles C Thomas, Publisher, Springfield, Ill., 1928.
11. Dandy, W. E. Venous abnormalities and angiomas of brain. *Arch. Surg.*, 1928, *17*, 715–793.
12. Dowling, J. L. Cerebral angiography in neurosurgery; angiographic appearances in cerebral tumors. *Australian & New Zealand J. Surg.*, 1950, *20*, 11–19.
Cerebral angiography in neurosurgery; angiographic appearances in intracranial aneurysms. *Australian & New Zealand J. Surg.*, 1950, *20*, 20–24.
13. Egas Moniz. L'encéphalographie artérielle, son

importance dans la localisation des tumeurs cérébrales. *Rev. neurol.*, 1927, *2*, 72–90.

14. EGAS MONIZ. Injections intracarotidiennes et substances injectables opaques aux rayons X. *Presse méd.*, 1927, *35*, 969–971.
15. FALCONER, M. A. Surgical treatment of bleeding intracranial aneurysms. *J. Neurol., Neurosurg. & Psychiat.*, 1951, *14*, 153–186.
16. HOLMAN, E. F. Physiology of arteriovenous fistula. *Arch. Surg.*, 1923, *7*, 64–82.
17. MOUNT, L. A. Treatment of spontaneous subarachnoid hemorrhage. *J.A.M.A.*, 1951, *146*, 693–698.
18. NORLÉN, G. Arteriovenous aneurysms of brain; report of 10 cases of total removal of lesion. *J. Neurosurg.*, 1949, *6*, 475–494.
19. OLIVECRONA, H., and RIIVES, J. Arteriovenous aneurysms of brain. *Arch. Neurol. & Psychiat.*, 1948, *59*, 567–602.
20. PADGET, D. H. Development of cranial arteries in human embryo. *Contrib. Embryol.* (No. 207–212), 1948, *32*, 205–262.
21. PILCHER, C. Cerebral vascular disorders in neurosurgery. *Bull. Tulane M. Fac.*, 1949, *8* 33–43.
22. REID, M. R. I. Studies on abnormal arteriovenous communications, acquired and congenital; report of series of cases. *Arch. Surg.*, 1925, *10*, 601–638.
    II. Abnormal arteriovenous communications, acquired and congenital, origin and nature of arteriovenous aneurysms, cirsoid aneurysms and simple angiomas. *Arch. Surg.*, 1925, *10*, 996–1009.
    III. Abnormal arteriovenous communications, acquired and congenital; effects of abnormal arteriovenous communications on heart, blood vessels, and other structures. *Arch. Surg.*, 1925, *11*, 25–42.
23. RUGGIERO, G., and CASTELLANO, F. Carotid-cavernous aneurysm. *Acta radiol.*, 1952, *37*, 121–140.
24. SCHWARTZ, H. G. Subarachnoid hemorrhage and intracranial aneurysm. *Postgrad. Med.*, 1948, *4*, 307–314.
25. SCOTT, W. G., and MOORE, S. Rapid automatic serialization of x-ray exposures by rapidograph, utilizing roll film nine and one-half inches wide. *Radiology*, 1949, *53*, 846–858.
26. SCOTT, W. G., and SEAMAN, W. B. Developments in cerebral angiography with rapid serialized x-ray exposures on roll film 9½ inches wide. *Radiology*, 1951, *56*, 15–30.
27. SHUMACKER, H. B., JR., Aneurysms and arteriovenous fistulas. *J. Michigan M. Soc.*, 1951, *50*, 168–173.
28. STREETER, G. L. Development of venous sinuses of dura mater in human embryo. *Am. J. Anat.*, 1915, *18*, 145–178.
29. SUGAR, O. Symposium; intracranial vascular abnormalities; pathological anatomy and angiography of intracranial vascular anomalies. *J. Neurosurg.*, 1951, *8*, 3–22.
30. TORKILDSEN, A., and KOPPANG, K. Notes on collateral cerebral circulation as demonstrated by carotid angiography. *J. Neurosurg.*, 1951, *8*, 269–278.
31. VIRCHOW, R. Ueber Naevi vasculosi des Gehirns. *Virchows Arch. f. path. Anat.*, 1864, *30*, 272.
32. WECHSLER, I. S., GROSS, S. W., and COHEN, I. Arteriography and carotid artery ligation in intracranial aneurysm and vascular malformation. *J. Neurol., Neurosurg. & Psychiat.*, 1951, *14*, 25–34.
33. WICKBOM, I. Angiographic examination of intracranial arterio-venous aneurysms. *Acta radiol.*, 1950, *34*, 385–398.

DISCUSSION

DR. CURTIS H. BURGE, Houston, Texas. I was glad that Dr. Scott emphasized the fact that good intracranial angiograms can be obtained with conventional equipment and that his rather elaborate biplane apparatus utilizing two roll film cassettes is not essential. A Fairchild roll film cassette was purchased for the Methodist Hospital here in Houston, but we have stopped using it for intracranial angiography because of the poor quality of the roentgenograms as compared to those made with regular equipment. After seeing the good quality of Dr. Scott's films made with this same apparatus, I feel that this is probably our fault and that we simply have not worked out a satisfactory technique. Good quality anteroposterior and lateral films which are timed properly, preferably with the lateral in stereo, will usually give one the desired information. A biplane arrangement is desirable for cutting the number of necessary injections in half.

I have not yet used urokon for intracranial angiography mainly because the manufacturer's representative told me a few weeks ago that the company was not yet ready to recommend this product for that purpose. However, Dr. Scott has apparently used urokon for some time and his experience seems to indicate that it is no more dangerous than other similar media. His statement that it produces fewer unfavorable reactions is certainly borne out in my own limited experience with this material for excretory urograms. In the past we always had an emesis basin and cold towel handy for use of one or both after every injection of another material, but except for nausea in an occasional case, the patients do not seem to

complain of any sensation whatever from an injection of urokon. Thorotrast still seems to be the best medium when the open method is used, but it should not be used for percutaneous injections because of the very painful reaction which occurs when it is accidentally injected into the tissues of the neck. The neurosurgeons in Houston have been converted almost completely to the percutaneous method so that we are using thorotrast only rarely at the present time.

Dr. Scott (closing). Dr. Burge's experience with the roll film cassette is familiar to those of us who worked with the early units. These difficulties occurred almost exclusively in the early models which did require considerable adjustment. The newer models are much better and work quite satisfactorily. The radiologists who obtained the earlier models and who are still having difficulty should have their local service technician return them to the factory. The Fairchild Company has announced that they are glad to check them over and recommend that the earlier models be equipped with their synchontrol timing device.

I would also like to point out that the operation of any new equipment, and particularly the roll film cassettes, requires a short period of operation to "break it in." Likewise, the technicians are not familiar with the use of this equipment or in the processing of the roll film which necessitates some training in both these respects.

The injections into the internal carotid artery were performed by both the percutaneous method and by direct injection into the surgically exposed vessel. The decision as to which technique is used depends on the neurosurgeon or the physician who is making the injection. Urokon 30 per cent has now been used a sufficient number of times to indicate that it is a satisfactory contrast medium for the visualization of the intracranial vessels.

VOL. 71, NO. 5

ROENTGEN RECOGNITION OF PARATHYROID ADENOMA*

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HYPERPARATHYROIDISM is a well known disease and has been discussed at length in previous presentations,[1,2,3,4,5,7,8] but there is little available information concerning the roentgen localization of the parathyroid tumor, adenoma, or hyperplasia per se.[1a] Hyperplasia, cystic changes, or carcinoma of the parathyroid gland may produce the same roentgenologic appearance as a parathyroid adenoma. It has been found that 10 per cent of patients having hyperparathyroidism have primary hyperplasia and hypertrophy of the glands, while 90 per cent have an adenoma. Of the patients with parathyroid adenomas, about 10 per cent will have two adenomas.[6] The present discussion is confined to the parathyroid adenoma and the roentgen recognition of its location.

It is highly important that the radiologist be aware that it is possible in many instances to accurately localize these lesions. Success in accomplishing this objective has a twofold advantage: (1) guiding the surgical approach, and (2) suggesting the diagnosis in an early stage of the disease. Certain roentgen changes have proved of value in demonstrating with reasonable satisfaction the position of the tumor.

The first preoperative visualization of a parathyroid adenoma at the Massachusetts General Hospital was made early in 1939 (Fig. 1). Since that time, although not all patients have been examined roentgenologically, there have been increasing numbers in whom the neck has been studied in a search for similar tumors. Technique has improved constantly with the demand for further study from a simple examination consisting of a single roentgenogram to that which includes roentgenoscopy, a barium swallow, appropriate large and indicated spot roentgenograms. During the years 1943 through April, 1952, 57 parathyroid adenomas were surgically removed. (During the same period, 10 other adenomas of the parathyroid were found at postmortem examination.) In the present investigation, 23 of the cases treated surgically had to be discarded because the examination had been inadequate or because no roentgenograms were available for study. In 34, satisfactory roentgenographic studies were available and these were correlated with the surgical findings. In 20 cases the location of the adenoma could be diagnosed from the roentgenograms.

ROENTGEN DEMONSTRATION OF PARATHYROID ADENOMA

Fundamental Prerequisites. It is axiomatic that three conditions must be met in order to recognize the existence of a soft tissue mass in the neck: (1) The mass must have attained a certain minimum size. (2) It must be located in such manner that it impinges upon or displaces certain readily recognized structures on the roentgenogram, especially the trachea, esophagus, and lungs. (3) The examination must be as complete as possible, and this should include roentgenoscopy, spot roentgenograms with barium in the esophagus, and large conventional roentgenograms of good technical quality of the chest and lower neck.

Anatomy. Without attempting to go into detailed discussion of the roentgen anatomy of the neck, certain facts must be remembered if minimal alterations in normal structures are to be recognized. The trachea lies slightly to the right of the midline in

* From the Department of Radiology, Massachusetts General Hospital. This study is a part of a collaborative research project on hyperparathyroidism being conducted jointly with the Departments of Surgery and Pathology, supported by a grant in aid from the American Cancer Society (Massachusetts Division). Presented at the Fifty-third Annual Meeting, American Roentgen Ray Society, Houston, Texas, Sept. 23–26, 1952.

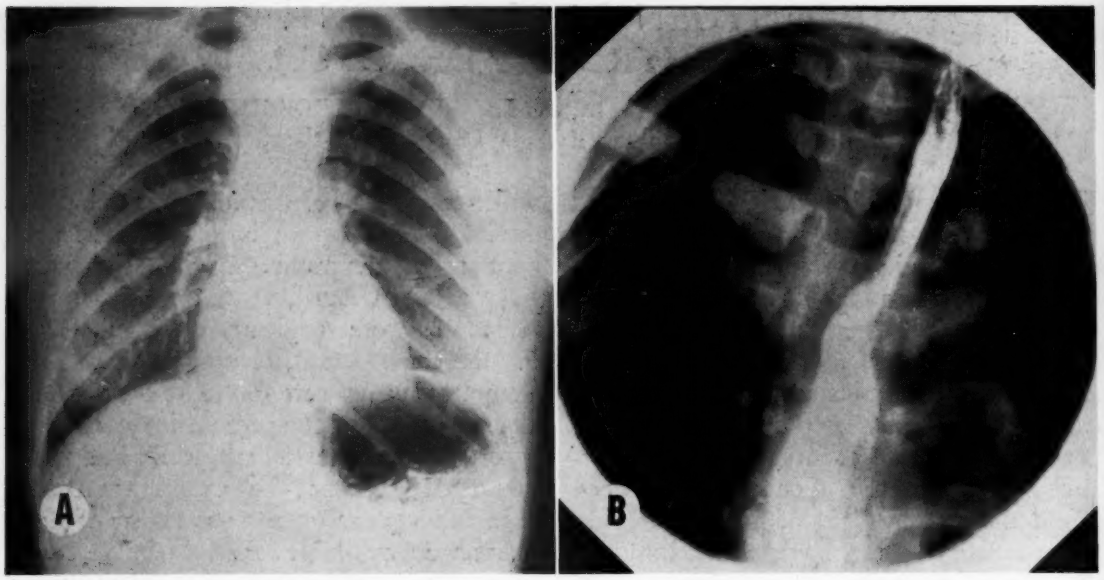

Fig. 1. Case 3. E. B. Female, aged twenty-two. A diagnosis of hyperparathyroidism had been established by laboratory studies five years before admission. There had been two unsuccessful explorations, and the patient had been given considerable roentgen therapy to the neck. At the time of this admission calcium was still elevated, phosphorus low, and the phosphatase was considerably increased.

(*A*) Posteroanterior roentgenogram demonstrates a mass in the lower neck and upper mediastinum outlined by air in the lung. (*B*) Spot roentgenogram shows indentation and displacement of the esophagus and trachea.

Operation: Because of the roentgen diagnosis, the lower portion of the right side of the neck was explored and, lying in a mass of scar tissue, a large tumor (6 by 3 by 1.5 cm.) was found and subtotally resected.

the lower neck and deviates a few millimeters more after entering the chest. The esophagus tends to be a midline structure in the neck but frequently shows a slight curve to the left before it enters the thorax. Both trachea and esophagus, however, normally follow a smooth course without significant indentations in the region of the neck. Therefore, minimal changes in the outline or course of these structures may be of great importance. Upon well grounded knowledge of this normal roentgen anatomy is the recognition of minor variations dependent.

Under normal circumstances the number and position of the parathyroid glands are extremely variable, but by and large they tend to be located in the substance of or adjacent to the capsule of the posterior portion of the right and left lobes of the thyroid gland. The parathyroid glands may lie in the mediastinum, especially in association with the thymus. In most instances, search for an enlarged parathyroid is made at the site where the thyroid is expected to lie. In this particular study, the vertebrae have been selected arbitrarily as landmarks for localization of these masses. Under usual circumstances of intrepretation, the lesion would probably be described in relation to the thyroid gland rather than to the spine.

Technique of Examination. From the technical standpoint, there are two approaches to the problem. One is by means of conventional reontgenograms and the second by means of roentgenoscopy and spot roentgenograms. A combination of these two methods is the ideal. Plain anteroposterior and lateral roentgenograms of the neck without contrast substance in the esophagus may be very informative. It is believed, however, that search for a parathyroid tumor should include careful roentgenoscopy with a barium swallow to outline the esophagus and that spot roentgeno-

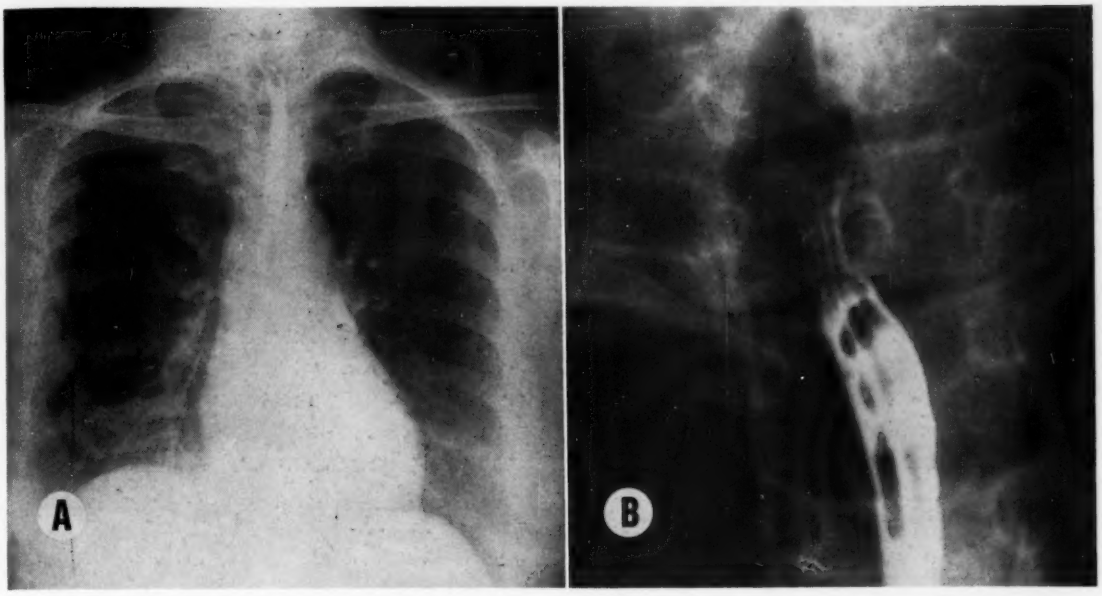

FIG. 2. Case 11. E. G. Female, aged fifty-three. Six months prior to admission the patient developed severe pain in the mandible and a biopsy showed a brown cystic tumor of the bone. She complained of lassitude, weakness, anorexia, polyuria, polydypsia, and low backache. Calcium 13.0, phosphorus 2.3, phosphatase 11.9.

(*A*) Posteroanterior roentgenogram shows indentation of the esophagus on the left with associated displacement. (*B*) Spot roentgenogram shows indentation on the left aspect of the lower cervical esophagus by a 2.5 cm. mass.

Operation: Behind the upper pole of the left lobe of the thyroid an adenoma was found which was approximately 3 cm. in length.

grams of the neck and upper mediastinum in the anteroposterior projection, both obliques, and in the lateral view if indicated, should be made. It is advisable also to take posteroanterior and lateral chest roentgenograms, and in this particular instance it is essential to include the neck. The lateral projection employed is similar to that which is employed when looking for a substernal extension of the thyroid,—that is, with the patient's hands joined posteriorly and held as low as possible.

Roentgen Diagnostic Signs. The most significant finding is one that is rare; that is, actual demonstration of the outline of a soft tissue mass (see Fig. 1). In the majority of cases only secondary evidence is available, manifested by indentation of the esophagus, trachea, or both. (A few parathyroid adenomas have been recognized by palpation prior to operation.) Localized indentation of the trachea on either side or posteriorly, or a localized indentation of the barium-filled esophagus laterally, anteriorly, or posteriorly are common and necessary signs. The degree of deformity or displacement of these structures will depend upon the size and location of the tumor. Occasionally a tumor will attain such size and extend sufficiently low into the thorax as to be outlined laterally by adjacent lung. In one-third of the cases in which the parathyroid adenoma was recognized, the indentation or displacement involved the trachea alone; in one-third, the esophagus alone; and in one-third, both trachea and esophagus (Fig. 2, 3 and 4). The indentation, whether of esophagus or trachea, was seldom visible when less than 1 centimeter in length; usually it was 2 to 3 cm., seldom greater than 6 cm. It is remotely possible that a tiny adenoma strategically placed against the esophagus could be recognized. The indentation due to a parathyroid adenoma is, as a rule, rather smooth. It is uncommon to find a lesion which suggests the

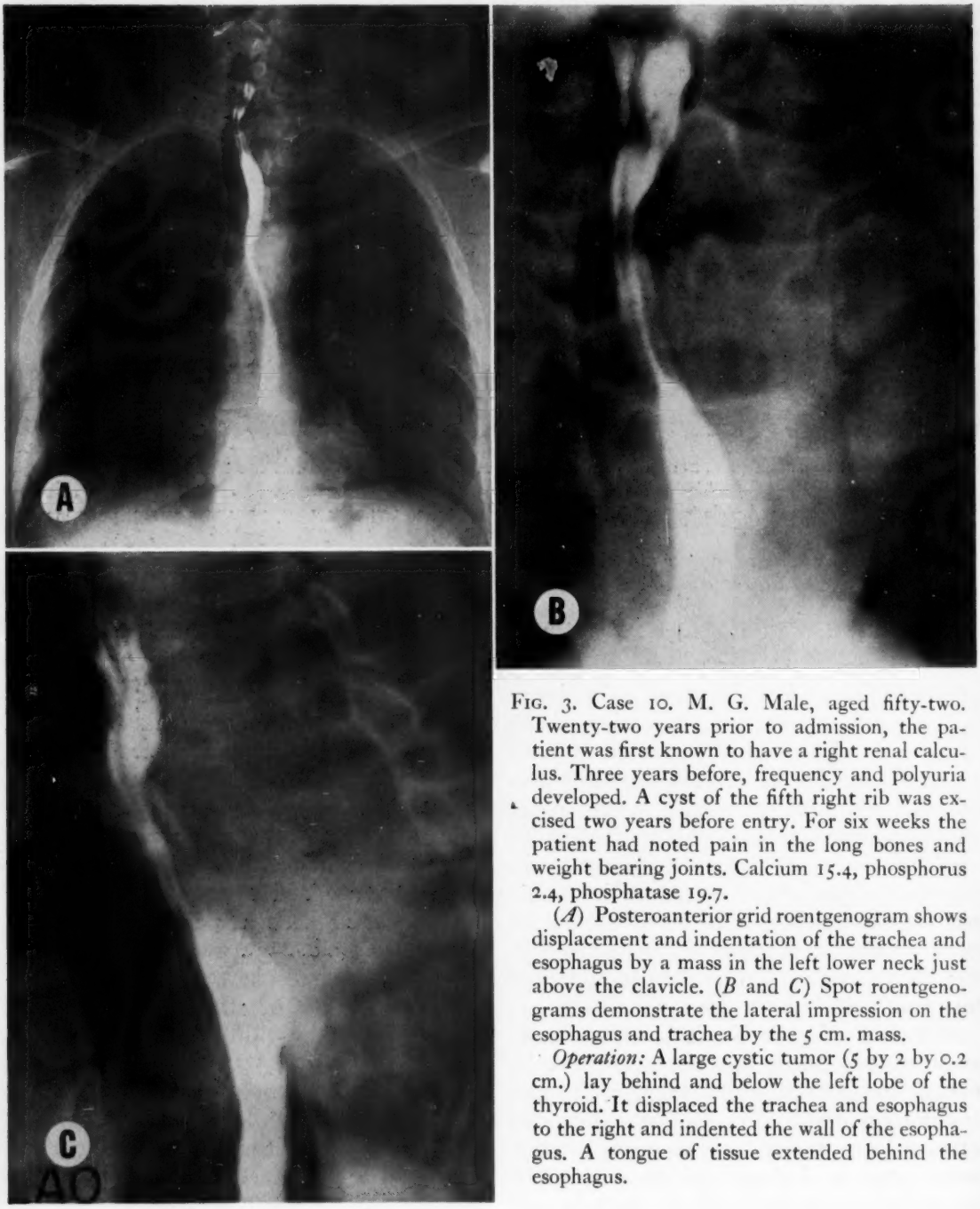

FIG. 3. Case 10. M. G. Male, aged fifty-two. Twenty-two years prior to admission, the patient was first known to have a right renal calculus. Three years before, frequency and polyuria developed. A cyst of the fifth right rib was excised two years before entry. For six weeks the patient had noted pain in the long bones and weight bearing joints. Calcium 15.4, phosphorus 2.4, phosphatase 19.7.

(*A*) Posteroanterior grid roentgenogram shows displacement and indentation of the trachea and esophagus by a mass in the left lower neck just above the clavicle. (*B* and *C*) Spot roentgenograms demonstrate the lateral impression on the esophagus and trachea by the 5 cm. mass.

Operation: A large cystic tumor (5 by 2 by 0.2 cm.) lay behind and below the left lobe of the thyroid. It displaced the trachea and esophagus to the right and indented the wall of the esophagus. A tongue of tissue extended behind the esophagus.

FIG. 4. Case 16. S.S. Male, aged forty-nine. The patient first passed ureteral stones twenty-six years before admission. During the year prior to entry he had had increasing headaches and had lost 20 pounds in weight. A mass, which had grown progressively, was palpable in the right lower neck; it moved with the trachea on swallowing. Calcium 13.0, phosphorus 5.4, phosphatase 15.0. There was associated bone disease as well as bilateral renal calculi.

Spot roentgenogram shows the trachea indented posteriorly and separated from the esophagus by the mass.

Operation: A 6.5 by 4 by 2 cm. mass was found behind the right lobe of the thyroid.

presence of an intramural extramucosal tumor of the esophagus (Fig. 5). In all instances, the tracheal indentation gives the impression of extrinsic pressure.

As will be noted in Table 1, these defects are most frequently seen at the projected level of the seventh cervical to the second thoracic vertebra. The size of the mass, as estimated by roentgenologic examination, varied from a diameter of approximately 1.5 cm. to 7 cm.; the majority of the recognized tumors were estimated to measure 3 cm.

The surgical and pathologic correlation of the localization and size of the adenomas corresponded in most instances very closely with the roentgenologic. It has not been possible to identify with certainty these masses as representing enlarged upper or lower parathyroid glands. A review of the operative notes on these patients has made it apparent that in many cases this could not be determined even at the time of surgical extirpation. It is quite possible that an enlarged upper parathyroid gland is less likely to be recognizable by virtue of its location close to the thyroid cartilage.

Of the 14 cases in which the adenoma was not recognized roentgenologically, 8 measured 1 cm. or less in maximum diameter; it is believed that tumors measuring less than 1 cm. are not likely to be visualized.

FIG. 5. Case 13. L. McA. Female, aged fifty-six. Two years before admission, a roentgenogram taken after a fall showed a cystic lesion in the left ilium. A year prior to entry, there had been a fracture of of the left side of the pelvis. The patient had noted increasing thirst for three or four years with associated frequency and nocturia. Calcium 14.2, phosphorus 2.5, phosphatase 26.5.

Spot roentgenogram shows displacement of the esophagus, and to a lesser extent the trachea, to the left and anteriorly. The deformity of the esophagus suggests that produced by an intramural extramucosal tumor.

Operation: A 6 by 4 by 2.5 cm. tumor was found behind the right lobe of the thyroid.

TABLE I

PARATHYROID ADENOMAS—ROENTGENOLOGICALLY VISUALIZED

Case No.	Sex	Age	Roentgenologic Findings	Location of Adenoma	Size of Adenoma
1	M	38	Esophagus displaced to rt. at level T-2 by mass 2.5 cm. ± in lt. lower neck	*Left*—Overlying and extending below inferior thyroid artery near lower pole	3×1.3×0.8 cm.
2	F	47	Minimal indentation trachea on lt. at level of T-1 by mass 3 cm. +	*Left*—At lower pole thyroid	4×3×1 cm.
3	F	22	A 7×3 cm. ± mass displaces trachea and esophagus to lt. at level T-1 to T-2	*Right*—At lower pole thyroid extending down to entrance of mediastinum	6×3×1.5 cm.
4	F	19	Minimal indentation on rt. side trachea at level T-1 to T-2	*Right*—Superimposed on middle thyroid vein, lateral to and behind upper pole thyroid	2.2×1.1×0.5 cm.
5	F	29	Esophagus displaced to rt. by mass 6 cm. ± at level T-1 to T-2	*Left*—Behind lower pole thyroid	3.5×2×0.5 cm.
6	M	48	On rt. side esophagus a 4 cm. indentation at level T-2 to T-3 displacing esophagus to lt. and post. Trachea indented on post. aspect. Mass between trachea and esophagus	*Right*—Behind rt. thyroid lobe, extending between esophagus and trachea	4×3.5×1.2 cm.
7	F	54	A 2 cm. nodule indents trachea on rt. at level of C-7 to T-1.	*Right*—Low in neck at upper border of sternum	2×1×1 cm.
8	F	47	Slight indentation trachea on rt. at level T-2	*Right*—Behind lower pole of thyroid	4×1×1.5 cm.
9	F	40	A 3 cm. mass indents esophagus on lt. at level T-1 to C-7	*Left*—Behind mid portion lt. thyroid lobe, lying against and adherent to esophagus	3 cm. diameter
10	M	52	A 5 cm. mass on lt. side indenting trachea and esophagus at level of T-1 to T-2	*Left*—Behind and below lt. lobe of thyroid	5×2×0.5 cm.
11	F	53	A 2 cm. mass indents esophagus on lt. at level T-1. No definite change in trachea	*Left*—Immediately behind upper pole left lobe thyroid	3 cm.
12	F	44	Trachea displaced slightly to rt. in low cervical region. Esophagus indented on lt.; displaced to rt. by 3 cm. mass level C-7 to T-1	*Left*—Behind inferior thyroid artery extending into thoracic strait	4×1.5×2.3 cm.
13	F	56	A 6 cm. mass indents esophagus, to less extent trachea, on rt. at level C-7 to T-2, probably adherent to esophagus	*Right*—Behind lower pole rt. lobe of thyroid	6×4×2.5 cm.
14	M	55	A 2 cm. mass indents esophagus (not trachea) at level C-7 to T-2, quite far posteriorly	*Left*—Posteriorly between esophagus and cervical spine behind lt. side thyroid	4×2×1 cm.
15	F	53	A 4 cm. mass at level T-1 to T-2 indents esophagus; to lesser extent trachea, lying between them	*Right*—Behind rt. lobe thyroid, extending partially into mediastinum	3×2.5×1 cm.
16	M	49	A 5 cm. mass between trachea and esophagus pushes trachea forward indenting trachea more than esophagus at level T-1 to T-3	*Right*—Behind rt. lobe thyroid pushing trachea to left	6.5×4×2 cm.
17	F	60	At level T-1 to T-3 a 6 cm. mass behind and displacing esophagus and trachea to rt. and slightly anteriorly	*Left*—Posterior to lt. lobe thyroid close to esophagus	6.4×1.3 cm.
18	M	62	Minimal indentation of trachea on lt. at level C-5	*Left*—Just superior to mid thyroid vein on left	2×2.5×3 cm.
19	F	63	A 1.5 cm. indentation lt. side trachea at level T-1	*Left*	—
20	F	57	A 5 cm. indentation lt. side trachea at level C-7 to T-3	*Left*—At lt. lower pole thyroid in superior mediastinum adherent to esophagus	4.5×2.8×2.5 cm.

Another 5 may have been overlooked because they were not situated adjacent to the trachea or esophagus. One of the 14 unrecognized adenomas measured 3.5 cm. in diameter and lay behind the right thyroid lobe pressing against and indenting the esophagus. This adenoma was missed because the examination was inadequate in that the spot roentgenograms had been centered too low.

DIFFERENTIAL DIAGNOSIS

It has already been noted that hyperplasia, cystic changes, and carcinoma of the parathyroid glands may produce a roentgen appearance which is identical with that of one or more adenomas.

In the differential diagnosis of parathyroid adenoma, presumably one must consider such varying and even bizarre conditions as branchial cleft cyst, cystic hygroma, connective tissue tumors, diverticulum of the esophagus, and intramural extramucosal tumors. The more common conditions with which it has been confused are the indentations produced on the cervical esophagus by the cricopharyngeus muscle, whether it be normal or hypertrophied, and an enlarged thyroid. It is quite conceivable that the normal cricopharyngeal muscular narrowing of the esophagus might be mistaken for enlargement of parathyroid glands. The symmetry of the defect produced by the cricopharyngeus muscle has a rather characteristic appearance and location which should make it readily recognized as normal. If enlarged, its being mistaken for symmetrical enlargement of two parathyroid glands is perhaps possible but unlikely. It is to be emphasized that enlargement of a lobe of the thyroid can produce an appearance which is identical with that of a parathyroid adenoma, and this is the major consideration in differential diagnosis. In consequence, it is necessary to take account of the laboratory findings that are typical of hyperparathyroidism,—namely, elevated blood calcium, low phosphorus, and sometimes elevated alkaline phosphatase. With an adenoma of the thyroid, calcification is commonly present whereas roentgenologic recognition of calcification of a parathyroid adenoma has not occurred in this series of cases. There have been, however, 2 cases in which calcification was present histologically.

CONCLUSIONS

1. In a series of thirty-four cases of surgically proved parathyroid adenomas, it was possible to localize the tumor roentgenologically in twenty.

2. The location of a parathyroid adenoma is commonly determined roentgenologically by changes from the normal detectable in the esophagus or trachea.

3. Preoperative localization of a parathyroid adenoma is important to guide the surgical approach.

4. Recognition of a parathyroid adenoma may lead to the correct diagnosis of hyperparathyroidism.

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REFERENCES

1. Albright, F., and Reifenstein, E. C., Jr. The Parathyroid Glands and Metabolic Bone Disease. Williams & Wilkins Company, Baltimore, 1948, (a) p. 102.
2. Black, B. K., and Ackerman, L. V. Tumors of parathyroid. *Cancer*, 1950, *3*, 415–444.
3. Castleman, B., and Cope, O. Primary parathyroid hypertrophy and hyperplasia; a review of 11 cases at the Massachusetts General Hospital. *Bull. Hosp. Joint Dis.*, 1951, *12*, 368–378.
4. Churchill, E. D., and Cope, O. Surgical treatment of hyperparathyroidism based on 30 cases confirmed by operation. *Ann. Surg.*, 1936, *104*, 9–35.
5. Cope, O. Endocrine aspect of enlargements of parathyroid glands. *Surgery*, 1944, *16*, 273–288.
6. Cope, O. Personal communication.
7. Norris, E. H. Collective review; parathyroid adenoma; study of 322 cases. *Internat. Abstr. Surg.*, 1947, *84*, 1–41.
8. Snapper, I. Medical Clinics on Bone Diseases. Second edition. Interscience Pub. Co., New York, 1949, pp. 73–74.

DISCUSSION

Dr. Aubrey O. Hampton, Washington, D.C. It is rather difficult to become critical after

hearing this paper and seeing the exhibit which Dr. Wyman and Dr. Robbins have. I always hate to discuss a paper that I can't criticize.

The authors did make one mistake, I think. The first parathyroid tumor was seen before 1939 but was not recognized. The patient was explored four times, when the tumor was finally recovered from his mediastinum. I think one reason I was asked to discuss this paper was that I might arise and make this remark. He was the famous ship captain that Albright and Cope reported.

I believe it is very important that we pay attention to what the authors have said, that the esophagus is displaced more than the trachea, usually, the trachea is displaced forward, in contradistinction to the much more common tumor of the thyroid.

The authors mention in their paper that the esophagus deviates normally to the left at just above the episternal notch. I have looked for tumors in the neck frequently, and have found this deviation, and it simulates a tumor very much. It is important that that normal variation be remembered.

In talking to these authors, they state—correctly, I think—that this curve is a more gentle sweep than the sharp indentation of a tumor.

It is true that we can add to the frequency of the diagnosis of parathyroid tumor if we find these tumor masses. Somebody must increase the frequency of the diagnosis. They are not all occurring in Boston, nor are they all occurring at the Mayo Clinic. The Mayo Clinic recently admitted that they had been missing a large number, and if you see their exhibit you will note that in the last ten years the incidence has gone up greatly out there.

We don't see many parathyroid tumors in Washington, for some reason or other.

Vol. 71, No. 5

THE PULMONARY ASPECTS OF POLYARTERITIS (PERIARTERITIS) NODOSA*

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DETROIT, MICHIGAN

THE roentgen appearance of the lung in polyarteritis nodosa is of equivocal nature. Only a few accounts have appeared in the literature, consisting of reports of one or several cases with positive lung findings. The present paper will offer a brief analysis of a group of proved cases of this disease, in all but one of which roentgen examinations of the chest were made. The clinical findings will be considered briefly and the pulmonary changes as determined roentgenographically will be assessed.

Periarteritis nodosa is the term coined by Kussmaul and Maier in 1866 to represent the pathological entity which they endeavored to describe.[10,20] Thirty-five years later Eppinger reviewed the microscopic sections and confirmed their findings. It is of further historical interest that von Rokitansky first described the microscopic lesions in 1852 under the title "The Formation of Aneurysms of the Arteries in General, except the Aorta and Most of its Primary Branches, with the Further Exception of the Cerebral Arteries." There is some reason for believing that the disease was recognized even earlier—in 1755 by Michaelis and Matoni and in 1810 by Pelleton, who reported a case in which he counted sixty-three small aneurysms of various arteries.[7]

Information accruing since the clinical and pathological recognition of the disease has helped somewhat to clarify the symptomatology, but theories of etiology have been many and varied. *Spirochaeta pallida*, streptococcic infections, virus infections, and parasites have been proposed as possible causes.[5,14] Some investigators believe that bacterial or other hypersensitivity is largely responsible for the disease.[15,16,17]

Because the term periarteritis nodosa did not satisfy maturing pathological and clinical conceptions of this disease, and because of information accumulated regarding pathology and pathogenesis, other names have been proposed, such as polyarteritis nodosa acuta, allergic arteritis, necrotizing panarteritis, essential polyarteritis and hypersensitive angiitis of Zeek.[23] Dickson,[3] in 1907, accepted Ferrari's term polyarteritis nodosa as a suitable one, since the process usually involves any or all of the vascular coats. Currently, polyarteritis nodosa is the designation generally accepted.

Polyarteritis nodosa is a destructive "inflammatory necrotizing" reaction of the vascular tree, involving principally the small arteries and arterioles in a segmental manner.[10] The lesions may be perivascular or may invade one or all of the vascular coats. Four stages of the process are described. The *degenerative stage* is characterized by edema and a fibrinous exudate about the inner elastic membrane, the muscle walls being separated by the exudate. In the *acute inflammatory stage* there is infiltration of the media and adventitia by polymorphonuclear leukocytes and eosinophils, followed by necrosis of the wall. Secondary thrombosis is first seen in this stage, and infarction of organs may result. The *stage of granulation or repair* is characterized by a change of polymorphonuclears and eosinophils to a round cell infiltration, with fibroblastic proliferation. The *healed stage* is seen as scar formation in the areas of involvement. Aneurysms, stenosis of vessels, and irregular nodules of scar tissue result. All stages may be seen in any one case.[1]

Arkin[1] lists the frequency with which various parts of the body are involved as

* From the Departments of Radiology and Respiratory Diseases, Henry Ford Hospital, Detroit, Michigan. Presented at the Fifty-third Annual Meeting, American Roentgen Ray Society, Houston, Texas, Sept. 23–26, 1952.

follows: kidneys, 80 percent; heart, 70 per cent; liver, 65 per cent; gastrointestinal tract, 50 per cent; pancreas, 25 per cent; mesenteric artery, 30 per cent; muscles, 30 per cent; peripheral nerves, 20 per cent; central nervous system, 8 per cent. Lung involvement is minimized by Arkin and by a number of others.[6,8,11] Harris *et al.*,[7] on the other hand, found the lungs involved in 25 per cent of the cases. Spiegel[20] reported the incidence of pulmonary involvement as 29 per cent, and Sweeney and Baggenstoss[22] as 28 per cent. Zeek, Smith and Weeter[23] believe that the disease not infrequently affects the systemic arteries in the lungs (the bronchial arteries) but that involvement of the pulmonary arteries and arterioles is rare in true polyarteritis nodosa though common in hypersensitive angiitis. They consider these two conditions separate entities by reason of their method of production and pathological characteristics, though both are part of an all-inclusive arterial disease which they call necrotizing panarteritis.

The real clinical characteristic of polyarteritis nodosa has been said to be "a disproportion between the number and severity of the symptoms and the disease which is assumed to be the cause."[7] The clinical manifestations depend upon which anatomic system or systems are involved, and there is consequently no typical course. The condition is characterized by varying symptoms in different locations, with periods of remission and exacerbation. Any or all organs may be involved. The diverse symptoms appear against a background of serious illness, with pallor, fever, rapid pulse, weight loss, pain and weakness in the extremities, renal and myocardial insufficiency, digestive disturbance, visual defects, and cutaneous lesions.[10] Because of these factors many cases are not recognized.[12] Life may terminate at any time as a result of such complications as thrombosis, gangrene, hemorrhage, or insufficiency of vital organ. The average duration of illness is from a few weeks to five months.[10]

Herrman[9] and von Conta,[2] in 1933, each reported one case which showed positive roentgen changes in the lungs, confirmed by postmortem examination. There was diffuse infiltration extending out from the hilar areas to the mid-clavicular line. In some areas confluent changes were seen, which were found to be infarcts. Von Conta's patient had nodules of various sizes in the lungs. Svanberg[21] described 3 cases with pulmonary involvement. In 2 there was increased vascular striation which was coarse centrally but thinned out peripherally. There were also present vaguely delimited nodules about the size of grains of rice. In the third case the findings were much more pronounced, with prominent striations and larger nodules. All 3 patients showed evidence of heart failure. A case of polyarteritis with pulmonary cavitation was reported by Sandler, Matthews, and Bornstein.[18] These writers believed the changes to be due to involvement of the larger arteries, with areas of extensive infarction which led to necrosis and excavation. The final diagnosis was made postmortem. Elkeles and Glynn[4] reported 5 cases and described the roentgen signs as follows; enlargement of the hilar areas, mottling in the middle and lower lung fields, patchy infiltration, and, in the later stages, enlargement of the heart, and pleural effusion. Shanks and Kerley[19] describe butterfly or batwing areas of edema situated around both hili, leaving the peripheral areas normally translucent.

MATERIAL

The material forming the basis of the present study includes 19 cases of polyarteritis nodosa observed in the period 1943 to 1952. As of July, 1952, 11 patients have died and 9 postmortem examinations have been done. Seven of the 8 remaining patients are known to be living and deny symptoms. One patient, in whom the diagnosis was made in 1944, cannot be traced beyond 1947, at which time symptoms were absent. Fifteen patients were males. The age range was from two and a half to sixty-four years.

Three case reports exemplify the protean manifestations of the disease.

Case I. J.P., a white male, aged fifty-nine, was well until six months previously when he began to experience epigastric distress which had continued undiagnosed and unabated. Three weeks prior to admission he began to vomit after meals, and dyspnea, cough, hemoptysis and ankle edema developed. Eight years earlier the patient had been hospitalized for osteomyelitis and treated with sulfonamides.

Physical Examination. The temperature and respiratory rate were normal. The pulse was 120 per minute and the blood pressure 120/60. The lungs were clear. A rough systolic murmur was present along the left sternal border. The liver was enlarged. Pitting edema of the ankles was evident.

Laboratory Findings. Results of blood studies were as follows: Hemoglobin, 7.0 gm. per 100 cc.; red blood cells 2,420,000; white blood cells 5,750, with 77 per cent polymorphonuclears and 23 per cent small lymphocytes. The urine contained albumin (3 plus), 3 red blood cells, granular casts and numerous white blood cells per high power field. The nonprotein nitrogen was 188 mg. per cent. The cephalin cholesterol-flocculation was 4 plus.

Roentgen examination of the chest showed moderate cardiac enlargement and diffuse infiltration in the middle and lower portions of the lungs. Multiple nodules of varying sizes were scattered through both lung fields (Fig. 1).

Course. Twenty-four hours after admission dyspnea and substernal distress suddenly developed. The blood pressure was not obtainable. Death ensued within one-half hour. Generalized polyarteritis nodosa was found on autopsy and characteristic lesions were present in the bronchial arteries.

The brief duration of life after admission and the abrupt peripheral vascular collapse which preceded death were handicapping to diagnosis. The pulmonary abnormalities could have been interpreted as congestive in origin.

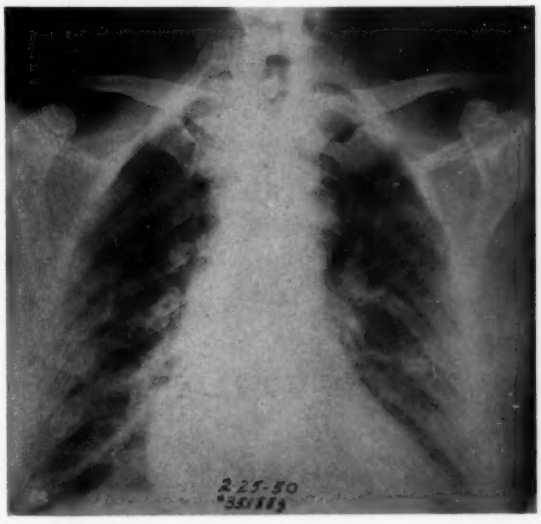

Fig. 1. Case I.

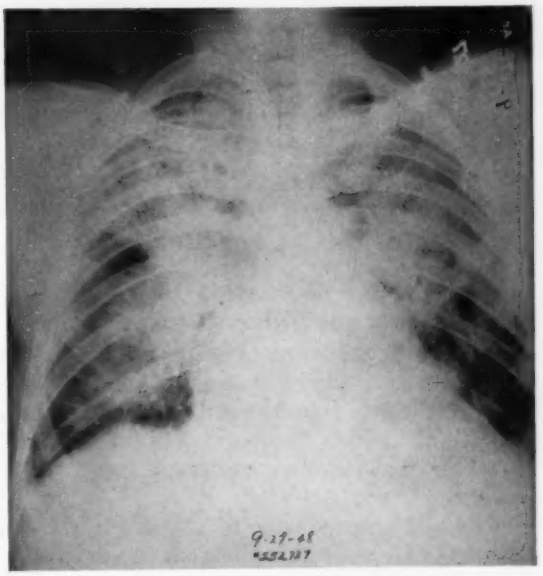

Fig. 2. Case II.

Case II. A.J., a white male, aged forty-one, complained of fatigue for two months associated with a 25 pound weight loss, ankle edema, dyspnea, and cough. Before admission he had noticed numbness of the hands and feet, had felt feverish, and had experienced episodes of tachycardia. He gave a history of syphilis twelve years previously, which responded well to routine treatment.

Physical Examination. The temperature and respiratory rate were normal. The pulse was 100 per minute and the blood pressure was 170/105. The lungs were clear. The heart was enlarged to the left, with protodiastolic gallop. The liver was enlarged. Pitting edema was present bilaterally.

Laboratory Findings. Hemoglobin was 10.5 gm. per 100 cc. The red blood cell count was 3,470,000, white blood cell count 13,000, with 81 per cent polymorphonuclears and 19 per cent small lymphocytes. Urinalysis showed

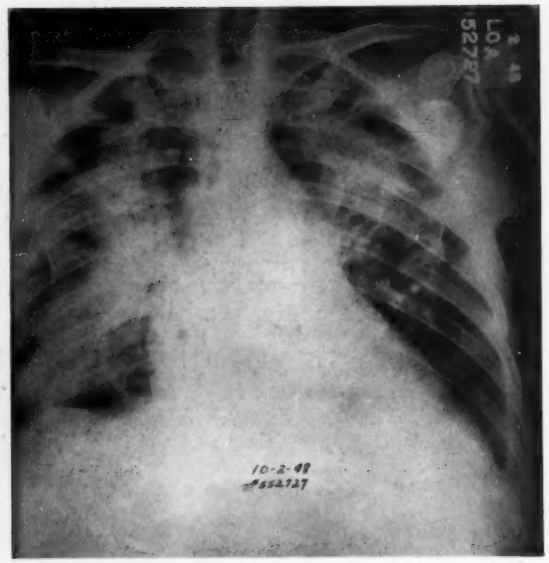

FIG. 3. Case II.

albumin 2 plus, a few red blood cells and granular casts per high power field. The nonprotein nitrogen was 52 mg. per cent. The sedimentation rate was 36 mm. in one hour. An electrocardiogram showed T waves inverted in leads of I and II and flat in lead III. Inverted T waves were present across the precordium from lead V 2 to lead V 6.

Roentgen examination of the chest showed batwing-like areas of infiltration in both lungs, most prominent in the central lung fields (Fig. 2). There was slight clearing in six days (Fig. 3).

Course. During the hospital stay shortness of breath became progressively worse. An acute episode of abdominal pain occurred, with right upper quadrant tenderness and rigidity, associated with a leukocyte count of 24,000. This subsided in four days. Death occurred on the nineteenth hospital day. Generalized polyarteritis nodosa was found on autopsy, with characteristic lesions in the bronchial arteries.

CASE III. W.A., a white male, aged fifty-seven, was admitted with generalized muscle pain of two weeks' duration, associated with a 13 pound weight loss, night sweats, fever and malaise.

Physical Examination. The patient appeared chronically ill. The temperature was 99° F., pulse 80 per minute, and respiratory rate 16 per minute. The blood pressure was 160/90. The liver was felt 3 cm. below the right costal margin. The calf muscles and testicles were tender; the lungs and heart appeared normal.

Laboratory Findings. Blood studies showed hemoglobin 12.6 gm. per 100 cc., red blood cells 4,260,000, white blood cells 13,000, with 74 per cent polymorphonuclears, 24 per cent small lymphocytes, and 2 per cent eosinophils. A trace of albumin, hyaline casts, a few red blood cells and 7 or 8 white blood cells per high power field were found in the urine. Bromsulfalein was retained in the liver, 22 per cent in forty-five minutes and 21 per cent in sixty minutes. The sedimentation rate was 40 mm. in one hour.

Roentgen examination of the chest on January 24, 1950, showed hilar enlargement with increased bronchovascular markings (Fig. 4). Later examination, March 6, 1950, showed marked hilar enlargement with extensive bilateral parenchymal infiltration most prominent in the upper lobes, and with evidence of nodulation (Fig. 5). These changes progressed and on March 17 there was generalized infiltration with pleural reaction and fluid on the right (Fig. 6).

Course. The hospital course was slowly but steadily retrogressive. Muscle pain persisted. Paresthesia developed in all extremities along with progressive paralysis and wasting of the legs. Urinary retention occurred. The sensorium was clouded. Testicular pain became severe. A cough developed, productive of mucoid sputum.

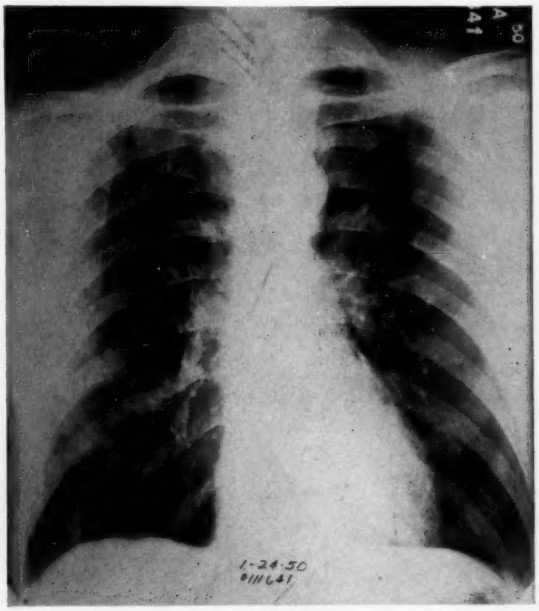

FIG. 4. Case III.

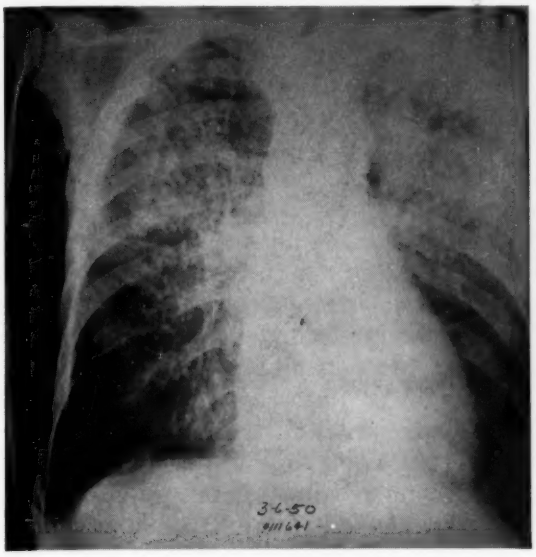

FIG. 5. Case III.

Hemoptysis occurred once. Low grade fever persisted, as did the leukocytosis and episodes of tachycardia. The blood pressure fluctuated between 140/80 and 160/90. One week prior to death, which occurred on the eighty-second hospital day, congestive heart failure supervened. Generalized polyarteritis nodosa was found at autopsy, with characteristic lesions in the pulmonary arteries.

The major features of the 19 cases were as shown in Tables I and II.

While 9 patients came to autopsy, in 7 of the 11 who died, biopsy-diagnosis was made before death.

ROENTGEN FINDINGS

The general impression of those who have written on this subject is that the roentgen changes in the lungs in polyarteritis nodosa are not characteristic of the disease. There are, however, certain lung changes, which, when combined with the clinical picture, are highly suggestive and may indicate the true diagnosis, or confirm it.

TABLE I

MAJOR FEATURES IN 8 LIVING PATIENTS

Symptoms	
Chest pain	4
Hemoptysis	1
Dyspnea	1
Cough	0
Roentgen Findings	
Hilar enlargement	5
Parenchymal infiltration	1
Nodules	3?
Fluid	0
Pathology	
Biopsy positive	8

FIG. 6. Case III.

Of 8 patients in this series in whom pulmonary lesions were seen at postmortem, 6 showed roentgen evidence of lung involvement. In 1 case the roentgen examination was negative, and 1 patient was not examined roentgenographically. Of the 6 patients with positive roentgen findings, 1 was under observation for three years, with

TABLE II

MAJOR FEATURES IN 11 FATAL CASES

Symptoms	
Chest pain	4
Hemoptysis	8
Dyspnea	6
Cough	10
Roentgen Findings (10 cases only)	
Hilar enlargement	9
Parenchymal infiltration	8
Nodules	2
Fluid	2
Pathology (9 cases autopsied)	
Bronchial arteries	5
Pulmonary arteries	2
Both bronchial and pulmonary arteries	1
Pulmonary infarcts	2
Lungs negative	1

positive biopsy findings but no roentgen evidence of pulmonary lesions. Recently she entered the hospital with an acute exacerbation of the disease. On this admission marked batwing areas of infiltration and moderate cardiac enlargement were demonstrable roentgenographically. Death occurred eight weeeks later, and autopsy confirmed the roentgen findings in the lungs.

Analysis of the roentgen changes in the 6 cases with evidence of pulmonary involvement disclosed the presence of parenchymatous infiltration in all. In 2 the familiar batwing areas of infiltration were demonstrated. Two showed nodulation, moderately pronounced. In 4 cases the heart was moderately enlarged, and 2 had fluid in the pleural cavity.

In all of the 10 cases not confirmed by autopsy, positive biopsy findings were obtained. Two of this group died of clinically active polyarteritis nodosa, but roentgen studies were negative. Three patients had increased vascular markings with suggestive areas of nodulation. The remainder showed no significant chest findings.

In this series of cases the lung changes followed roughly the pattern described by earlier writers. There was moderate or pronounced hilar enlargement in most cases. The milder changes consisted of prominence of the linear markings throughout the lungs, with an occasional small localized density which is difficult to classify and which may or may not be significant. The more advanced lung changes consist of extensive areas of perivascular and parenchymal infiltration with some generalized haziness extending out from the hilar areas into the lung fields. The areas of involvement are not selective and occur in the upper lung fields nearly as frequently as in the bases. Several of our cases showed the typical batwing-shaped areas of infiltration spreading out from the hilar areas, with other areas of the lungs relatively clear. These areas often cleared to a considerable degree, but subsequently more pronounced changes developed, which persisted until death.

In a few cases there were small confluent areas of density suggesting nodulation. These varied in size from a few millimeters in diameter to a centimeter or more. They were associated with coarse linear markings and were more commonly present in the central portions of the lungs. Pleural fluid was not a common finding in this series but was present in 2 fatal cases.

The association of cardiac enlargement and pronounced lung changes is such as to suggest the possibility that the latter are congestive in nature. The batwing-shaped areas are similar to those seen in cases of chronic uremia, which typically involves the central portions of the lung and does not extend to the periphery. Allergy must also be considered as a distinct possibility in evaluating the possible causes of the pulmonary changes.

GENERAL DISCUSSION

Seven of the patients in this series are known to be living and without symptoms. The duration of life since biopsy diagnosis in 3 instances has been six years, in 1 four years, in 2 two years, and 1 is a current case. The remaining patient, unaccounted for since 1947, had a known remission of three years. In these patients pulmonary symptoms and roentgenological abnormalities were neither frequent nor helpful in diagnosis.

In the 2 patients who died but were not autopsied death occurred within one year after diagnosis by biopsy.

In the 9 patients who came to autopsy, death occurred within eight months after the onset of symptoms. Eight patients died of progressive disease with no remissions; 1 was well for three years after biopsy diagnosis and then died of an acute recurrence in eight weeks. All 9 of these cases showed pathological lesions of polyarteritis nodosa in one phase or another in a generalized distribution. Some cases showed lesions in all four phases of activity, according to Arkin.[1] *Seven showed lesions* in either the bronchial or pulmonary arteries, 1 in both. In all the fatal cases the appearance was that of progressive chronic illness, with in-

creasing pallor, weakness, and emaciation. All showed evidence of multiple systemic involvement. The cases having extensive roentgen changes in the lungs were found to have minimal and incompatible physical findings.

Pulmonary involvement, according to this series, indicates a poor prognosis. In the patients who died (Table II) pulmonary symptoms were frequent and handicapping. Roentgen abnormalities, especially parenchymal infiltration, were evident. Pulmonary vascular involvement (bronchial, pulmonary or both) was present in all autopsy specimens, except one.

Two patients were treated with cortisone, with apparent resolution of parenchymal infiltration, but both subsequently died, one during treatment of a cerebral hemorrhage[13] and the other from an acute exacerbation of the disease one month after cortisone was discontinued.

SUMMARY

1. Nineteen proved cases of polyarteritis nodosa are reported.

2. Eight autopsied cases showed characteristic lesions in pulmonary or bronchial arteries or in both.*

3. Roentgenological pulmonary abnormalities were present in six cases. These findings are not specific but may be suggestive.

4. Major pulmonary symptoms or parenchymal roentgenological abnormalities indicate a poor prognosis.

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REFERENCES

1. ARKIN, A. Clinical and pathological study of periarteritis nodosa; report of five cases, one histologically healed. *Am. J. Path.*, 1930, *6*, 401–426.
2. VON CONTA, G. Periarteriitis nodosa der Lungengefässe und Lungenröntgenbild. *Fortschr. a. d. Geb. d. Rontgenstrahlen*, 1933, *47*, 506–510.
3. DICKSON, W. E. C. Polyarteritis acuta nodosa and periarteritis nodosa. *J. Path. & Bact.*, 1908, *12*, 31–57.
4. ELKELES, A., and GLYNN, L. E. Serial röntgenograms of chest in periarterits nodosa as aid to diagnosis, with notes on pathology of pulmonary lesions. *Brit. J. Radiol.*, 1944, *17*, 368–373.
5. FRIEDBERG, C. K., and GROSS, L. Periarteritis nodosa (necrotizing arteritis) associated with rheumatic heart disease, with note on abdominal rheumatism. *Arch. Int. Med.*, 1934, *54*, 170–198.
6. GRIFFITH, G. C., and VURAL, I. L. Polyarteritis nodosa; correlation of clinical and postmortem findings in 17 cases. *Circulation*, 1951, *3*, 481–491.
7. HARRIS, A. W., LYNCH, G. W., and O'HARE, J. P. Periarteritis nodosa. *Arch. Int. Med.*, 1939, *63*, 1163–1182.
8. HERBUT, P. A., and PRICE, A. H. Periarteritis nodosa producing aneurysm of renal artery and hypertension. *Arch. Path.*, 1945, *39*, 274–278.
9. HERRMAN, W. G. Pulmonary changes in case of periarteritis nodosa. AM. J. ROENTGENOL. & RAD. THERAPY, 1933, *29*, 607–611.
10. KERNOHAN, J. W., and WOLTMAN, H. W. Periarteritis nodosa; clinicopathologic study with special reference to nervous system. *Arch. Neurol. & Psychiat.*, 1938, *39*, 655–686.
11. LICHTMAN, A. L., STICKNEY, J. M., and KERNOHAN, J. W. Periarteritis nodosa; report of case. *Proc. Staff Meet, Mayo Clin.*, 1943, *18*, 500–504.
12. MIDDLETON, W. S., and MCCARTER, J. C. Diagnosis of periarteritis nodosa. *Am. J. M. Sc.*, 1935, *190*, 291–308.
13. REEDER, W. H., and GOODRICH, B. E. Pulmonary infiltration with eosinophilia (PIE Syndrome). *Ann. Int. Med.*, 1952, *36*, 1217–1240.
14. REIMANN, H. A., PRICE, A. H., and HERBUT, P. A. Trichinosis and periarteritis nodosa; differential diagnosis; possible relationship. *J.A.M.A.*, 1943, *122*, 274–279.
15. RICH, A. R. Role of hypersensitivity in periarteritis nodosa as indicated by 7 cases developing during serum sickness and sulfonamide therapy. *Bull. Johns Hopkins Hosp.*, 1942, *71*, 123–140.
16. RICH, A. R., and GREGORY, J. E. Experimental demonstration that periarteritis nodosa is manifestation of hypersensitivity. *Bull. Johns Hopkins Hosp.*, 1943, *72*, 65–88.
17. RICH, A. R. Hypersensitivity to iodine as cause of periarteritis nodosa. *Bull. Johns Hopkins Hosp.*, 1945, *77*, 43–48.
18. SANDLER, B. P., MATTHEWS, J. H., and BORNSTEIN, S. Pulmonary cavitation due to polyarteritis. *J.A.M.A.*, 1950, *144*, 754–757.
19. SHANKS, S., and KERLEY, P. A Textbook of X-Ray Diagnosis, By British Authors in Four

* The study of pathological material was conducted by Dr. Frank W. Hartman and Dr. Ira Gore, to whom we are greatly indebted.

Volumes. Second edition. W. B. Saunders Company, Philadelphia, 1950, Vol. 2, p. 171.
20. SPIEGEL, ROSE. Clinical aspects of periarteritis nodosa. *Arch. Int. Med.*, 1936, *58*, 993–1040.
21. SVANBERG, T. Roentgenographical pulmonary changes in periarteritis nodosa. *Acta radiol.*, 1945, *26*, 307–312.
22. SWEENEY, A. R., and BAGGENSTOSS, A. H. Pulmonary lesions of periarteritis nodosa. *Proc. Staff Meet., Mayo Clin.*, 1949, *24*, 35–43.
23. ZEEK, PEARL M., SMITH, C. C., and WEETER, J. C. Studies on periarteritis nodosa; differentiation of periarteritis nodosa and of hypersensitivity. *Am. J. Path.*, 1948, *24*, 889–917.

DISCUSSION

DR. VINCENT W. ARCHER, University, Virginia. Dr. Doub and his co-workers have as usual presented a fine discussion of the clinical, roentgenologic and pathologic factors of the condition commonly described as periarteritis nodosa. This syndrome exemplifies so many of our medical problems, etiology unknown, treatment empirical, prognosis guarded.

As the authors have pointed out, there is nothing definitely pathognomonic in the roentgenological findings. On the other hand, if the radiologist has a full clinical history, and observes the pulmonary changes as described, he can and should suggest the possibility of periarteritis or of some of the other closely similar conditions.

In going over the most recent literature relevant to this subject, a most interesting and thought-provoking paper by Bauer, Giansiracura and Kulka was found in "Rheumatic Diseases," a group of papers presented at the Seventh International Congress on Rheumatic Disease. In this article the clinical manifestations of connective tissue disease are tabulated (Chart 1) and the overlap is quite prominent. In the discussion of individual cases, these authors point out that the clinical features overlap to such an extent that diagnosis is very difficult or impossible in many instances. They show that in some cases, even with complete postmortem examination, the diagnosis could

Clinical Manifestations of Connective Tissue Diseases

	CONSTITUTIONAL	VASOMOTOR	CHOREA	OCULAR	SKIN	PURPURA	MUCOUS MEMBRANES	LYMPHADENOPATHY	SPLENOMEGALY	CARDIAC	HYPERTENSION	PULMONARY	GASTRO INTESTINAL	ARTHRITIS	NODULES	MUSCLES	PERIPHERAL NERVES	EOSINOPHILIA	RENAL	W.B.C.
RHEUMATOID ARTHRITIS	+	+	O	+	+	+	O	+	+	+	O	O	O	+	+	+	+	+	⊕	↑
RHEUMATIC FEVER	+	+	+	+	+	+	O	O	+	+	O	+	+	+	+	=	O	O	+	↑
LUPUS ERYTHEMATOSUS DISSEMINATUS	+	+	±	±	+	+	+	+	+	+	+	+	O	+	+	+	O	O	+	↓
PERIARTERITIS NODOSA	+	+	O	O	+	+	O	+	+	+	+	+	+	+	+	+	+	+	+	↑
DERMATOMYOSITIS	+	+	O	O	+	±	±	+	+	+	O	O	−	+	+	+	O	+	±	↑
SCLERODERMA	±	+	O	O	+	O	O	O	O	+	O	+	+	+	O	+	O	O	O	N

The + sign indicates those findings seen with some regularity in a large series of patients but implies nothing as to frequency or severity. The ± sign refers to features rarely encountered. The ⊕ indicates an extremely rare finding. The 0 signifies that this particular finding has been absent in our experience or cannot be attributed directly to the disease under consideration. The squares indicate prominent or characteristic features of each disease. The frequency with which the leukocyte counts deviate from normal (N) is indicated grossly by the size of the arrows: ↑ = leukocytosis, ↓ = leukopenia.

(from Bauer, Giansiracusa, and Kulka)

CHART I*

* Reproduced, by permission, from Bauer, Walter, Giansiracura, J. E., and Kulka, J. P. The Protean Nature of the Connective Tissue Diseases. Rheumatic Diseases. W. B. Saunders Company, Philadelphia, 1952, pp. 391–400.

not be narrowed either clinically or pathologically to one of the group of connective tissue diseases. They further state, however, "Since these diseases differ in clinical pattern and prognosis, the generally accepted terminology serves a useful purpose."

It would seem, therefore, that whatever the possible common causative relationship, the recognition of one particular variant will be quite helpful in prognosis, and the radiologist as a clinical consultant should play an important role. The authors have performed a valuable service in calling this syndrome to our attention.

MULTIPLE PRIMARY CARCINOMAS OF THE LARGE INTESTINE*†

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MULTIPLE primary malignant tumors are not rare. Earlier writers believed that the occurrence of more than one independent malignant neoplasm in an individual was merely accidental coincidence.[13] It has been shown, however, that multiple tumors develop more often than would be expected on the basis of chance alone.[8,27] This is a significant fact insofar as the large intestine is concerned, because cancer of the colon and rectum is probably the most common form of cancer in males and the third most frequent in females.[12] Furthermore, there is an excellent chance of cure if the diagnosis is made early.

The majority of reports have dealt with multiple primary malignant tumors involving various organs or structures. Although a number of excellent papers devoted exclusively to the subject of multiple primary carcinomas of the large intestine have been published during the last few years,[1,2,7,18,19,22,23,24,26] apparently very few have appeared in the radiologic literature.[18a]

Berson and Berger[4] state: "unquestionably many 'poor results' in the treatment of cancer of the large intestine can be attributed to the fact that a second lesion was missed." Investigations by Long, Mayo, Dockerty and Judd[18] indicate that a certain percentage of so-called "recurrent" lesions are not truly recurrences, but new and independent neoplasms.

The present report of multiple primary carcinomas of the colon and rectum is based on the review of the records of 812 patients who had surgical treatment for cancer of the large intestine at the Hospital of the University of Pennsylvania during the twelve year period 1940 to 1951. Of this group, 24 (2.9 per cent) had multiple primary carcinomas.

Patients who had diagnoses of familial polyposis or chronic ulcerative colitis were considered to have separate disease entities and were excluded. Polyps which showed malignant transformation were not regarded as distinct malignant tumors, unless the microscopic sections showed unquestionable invasive carcinoma.

REVIEW OF THE LITERATURE

Billroth,[5] in 1869, is generally credited with reporting the first case of multiple primary malignant tumors. He asserted that certain criteria must be fulfilled before a case could be included within the category of multiple primary cancers: each tumor must have a different histopathologic appearance; it must arise in a different location; each must produce its own metastasis. These postulates, which are now only of historical interest, excluded many true cases of multiple primary malignant neoplasms and have been supplanted by more liberal specifications.

In 1932, Warren and Gates[27] made an exhaustive study of multiple primary cancers. According to these authors, the strict criteria which had been employed to determine the authenticity of multiple primary malignancies up to that time had resulted in a falsely low incidence. Many tumors, particularly those arising in the same organ, such as the large intestine, were not admitted under Billroth's specifications. Today, the requirements given by Warren and Gates are those generally adhered to in deciding whether multiple malignant tumors represent true instances of primary cancers. Their criteria are as follows: each of the tumors must present a definite picture of malignancy; each must be distinct; and the probability of one being a metastasis of the other must be excluded.

Warren and Gates reviewed all of the cases of multiple malignancy reported in the litera-

* From the Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, with assistance from the Institutional Grant of the American Cancer Society and the Penn Mutual Life Insurance Foundation for the Study of Neoplastic Diseases.

† Presented at the Fifty-third Annual Meeting, American Roentgen Ray Society, Houston, Texas, Sept. 23–26, 1952.

ture up to the time of their publication (1932), and found 546 examples of multiple primary cancers among 29,740 cases of malignant disease—an over-all incidence of 1.84 per cent. In their own series of 1,078 autopsies performed in connection with cancer patients, there were 40 instances of multiple primary malignant neoplasms—an incidence of 3.7 per cent. They compared the actual versus the expected incidence of multiple primary malignant neoplasms based upon Massachusetts' cancer mortality statistics and concluded that the actual number of cases of multiple cancers was several times greater than that expected on the basis of chance alone. Bugher,[8] who analyzed Michigan's cancer mortality statistics, came to the same conclusion.

At the Wisconsin General Hospital, Burke[9] studied 583 cases of malignant disease and discovered 46 (7.8 per cent) instances of multiple lesions. There were 23 examples of primary multiple malignant lesions in a series of 306 cancer patients analyzed by Brindley;[7] 8 (2.6 per cent) of this series had multiple primary carcinomas of the colon. The highest incidence of multiple primary malignant lesions of the colon and rectum recorded to date is that of Berson and Berger,[4] who reported 16 (4.6 per cent) such cases in a group of 344 patients who had undergone surgical treatment of carcinoma of the large intestine.

To date, the most extensive published study of multiple primary carcinomas of the large intestine is that of Thomas, Dockerty and Waugh,[26] whose analysis was based on surgically removed specimens and on the records of 132 cases encountered at the Mayo Clinic during the years 1907 through 1944. These 132 patients represented approximately 3 per cent of all patients with cancer of the large intestine at the Clinic subjected to operation during the time in which the cases were encountered. These authors found that patients who had multiple primary malignant lesions of the colon and rectum were younger than patients who had single lesions—that there was an even greater preponderance of males—that the incidence 2f associated polyps was more than twice as great in the series of multiple malignant lesions than in a control group of single carcinomas. There was a puzzling difference in distribution when simultaneous and nonsimultaneous multiple carcinomas were compared. This subject will de discussed later. Thomas, Dockerty and Waugh concluded that the occurrence of multiple malignant neoplasms is a reflection of an inherent constitutional susceptibility to cancer that is present in some individuals. Their statistics also re-emphasized the importance of polyps of the colon in relation to carcinoma of the large intestine.

Investigations by Long, Mayo, Dockerty and Judd[18] indicate that nonsimultaneous multiple primary carcinomas of the large intestine are even more common than present statistics would lead us to believe. These collaborators undertook to determine whether patients with evidence of carcinomas in the region of previously resected malignant neoplasms had, in reality, recurrent or new and independent carcinomas. In their discussions, it is brought out by Dockerty that: "There are three ways by which carcinoma may reappear in the vicinity of an anastomotic site after removal from the large bowel of an original growth of the same type—(1) By continuation of the growth of cancer tissue which the surgeon inadvertently left behind—a part of the parent tumor or metastasis from it, (2) By way of malignant degeneration in a neighboring polyp, (3) Development of fresh cancerous changes from predisposed epithelium in the region of the original tumor. The tumors in the first group have a poor prognosis, while those in the second and third groups are amenable to surgery."

According to Long and his co-workers, modern pathologists believe the view earlier expressed by other authorities, that cancer is frequently multicentric in origin, that carcinomas may arise from large or small fields of tissue and enlarge not only by cellular proliferation but also by progressive neoplastic conversion of tissue within these fields. They state: "If this concept is true, then there should be a transition zone between a carcinoma of the colon and the surrounding adjacent mucosa." It would be present in new lesions but not in recurrent tumors.

This transition zone was found, and constituted the criterion by which Long, Mayo, Dockerty and Judd proposed to prove the authenticity of new and independent carcinomas in the area of a previously resected malignant lesion. They studied the operative specimens from 30 patients who had had resection of the bowel for so-called "*recurrent*" carcinomas. In their opinion, 21 of these 30 patients actually had true recurrences of the original tumor. These carcinomas, when they recurred, exhibited no transition zone between the carcinoma

and normal mucosa. In these cases, the outcome was very poor. The average time between operations was 2.9 years and the mean survival time was 1.5 years. Only 4 patients lived for three years after removal of the recurrent tumor and only 1 lived more than five years. Nine patients (almost one-third of the 30 patients) were thought to have *new and independent carcinomas*. The presence of a transition zone at the junction of the mucosa and the tumor was the basis for placing these 9 patients with 10 lesions in this group. Of these 9 patients, 2 died in the hospital and 1 who had a palliative resection was not traced. The mean survival rate for the other 6 patients was 5.4 years when last followed-up. The mean interval between operations was 4.1 years.

Long and his associates concluded that patients who are believed to have "*true recurrent*" malignant tumors of the large intestine should not be denied exploratory operation unless there is evidence of distant metastasis.

PRESENT SERIES

As previously stated, the records of 812 patients who underwent surgical treatment for cancer of the large intestine at the Hospital of the University of Pennsylvania during the twelve year period 1940 to 1951 were reviewed. Of these, 24 (2.9 per cent) had multiple primary carcinomas of the colon and rectum. As already stated, patients who had developed cancer secondary to familial polyposis or ulcerative colitis were not included. In order to conform with Warren and Gates' criterion that each tumor must present a definite picture of malignancy, only polyps which showed unquestionable invasive carcinoma, as demonstrated in the microscopic sections, were considered as separate carcinomas.

Sixteen patients (Table 1) had 34 simultaneous lesions (these have been called "synchronous" carcinomas by Thomas, Dockerty and Waugh[26]). The roentgenogram and pathologic specimen of a typical case (Case 5) are shown in Figure 1. Cases 9 and 16 each developed three simultaneous carcinomas. The roentgenograms in Case 8 showed two lesions, one in the rectum and another in the transverse colon; the rectal carcinoma was verified by proctoscopic biopsy but the tumor in the transverse colon was not confirmed pathologically. Exploration was not carried out in Case 14 because of pulmonary metastasis, but the roentgen findings were unequivocal (Fig. 2).

Eight patients had eighteen independent malignant neoplasms which developed at different times (metachronous carcinomas, or as they have been called by Thomas,

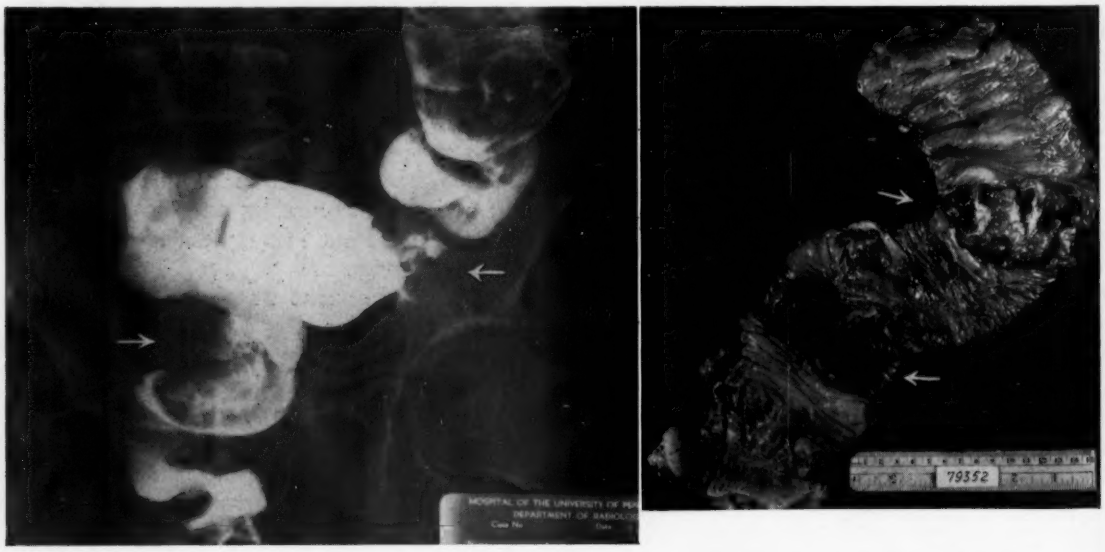

FIG. 1. Case 5. Roentgenogram and specimen showing two simultaneous carcinomas, one in the rectum and the other in the sigmoid.

FIG. 2. Case 14. Roentgenogram showing two simultaneous carcinomas, one in the sigmoid and the second in the ascending colon.

Dockerty and Waugh, "asynchronous" carcinomas). Case 17 had three separate carcinomas resected at different intervals. In Case 19 (Fig. 3) two simultaneous cancers were found three years subsequent to removal of a single carcinoma. Case 24 had resection for carcinoma of the sigmoid; twenty months later the patient was again operated upon because of recurrence of the original growth in the sigmoid. At this time, the surgeon also noted an independent carcinoma in the cecum.

Sex Incidence. It is well established that cancer of the large intestine is more prevalent in males. The records of 175 patients who underwent resection for single carcinomas of the colon and rectum at the Hospital of the University of Pennsylvania during the years 1950 and 1951 showed that 98 (56 per cent) were males and 77 (44 per cent) were females. Other writers have found an even greater preponderance of males in their series of multiple carcinomas when compared to control series of single carcinomas.[4,23,26] In our group with multiple cancers, however, there were 15 (62.5 per cent) females and 9 (37.5 per cent) males.

Age Incidence. Hanlon,[14] in 1931, observed that the occurrence of multiple primary malignant neoplasms was closely linked with advancing age because the average age of patients with multiple primary malignant tumors in his series was greater that that of individuals with single lesions. Subsequent writers have disagreed with Hanlon on this point. Warren and Gates,[27] in their large group, including various types of malignant tumors collected from the literature, found that there was no average age difference between patients with multiple and single lesions. They stated: "certainly, these cases have not developed their multiplicity of cancers because of a longer time during which additional tumors might make their appearance."

Berson and Berger[4] reported a series of 16 patients who were found to have multiple carinomas of the colon and rectum. The average age was 54.8 years as compared to the average age of 56.1 years in a

FIG. 3. Case 19. Roentgenogram showing a large carcinoma in the transverse colon and a polyp in the sigmoid. There is also a defect in the descending colon at the site of a previously resected carcinoma. Proctoscopic examination showed a rectal carcinoma.

TABLE I

MULTIPLE SIMULTANEOUS PRIMARY CARCINOMAS OF THE COLON, HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA 1940–1951

Case	Sex	Age yr.	Location of Lesions	Associated Polyps
1. F.B.	F	60	Rectum; sigmoid	Yes
2. S.B.	M	53	Rectum; sigmoid	No
3. M.B.	F	55	Rectum; sigmoid	Yes
4. M.C.	F	44	Rectum; sigmoid	Yes
5. A.D.	M	62	Rectum; sigmoid	No
6. E.E.	M	55	Rectum; rectosigmoid	Yes
7. B.G.	F	62	Ascending colon (2)	No
8. J.H.	M	77	Rectum; transverse colon	No operation
9. S.J.	F	54	Transverse colon (2) Descending colon (1)	Yes
10. B.L.	F	60	Sigmoid; transverse colon	No
11. N.M.	F	66	Sigmoid; transverse colon	No
12. L.P.	F	59	Descending colon (2)	No
13. A.S.	M	72	Rectosigmoid; sigmoid	Yes
14. A.S.	F	70	Sigmoid; ascending colon	No operation
15. G.V.	F	66	Ascending colon; rectum	Yes
16. S.W.	M	54	Sigmoid (3)	Yes

group of 344 cases of single cancers of the large intestine.

Mider's[19] records showed that 21 patients with multiple carcinomas of the large intestine averaged sixty-one years, while those with single lesions of the same viscus averaged sixty years.

Statistically, the most significant group reported is that of Thomas, Dockerty and Waugh.[26] The average mean age of 132 patients with multiple carcinomas of the large intestine at the Mayo Clinic was 54.7 years, while that of 475 patients with single carcinomas was 56.0 years. These authors concluded, as already referred to, that there is an inherent constitutional tendency toward the development of cancer, which is reflected in the younger age at which the disease occurs and in the development of subsequent primary lesions, if the patient survives.

Our records show that the average age of 175 patients with single carcinomas of the colon and rectum at the Hospital of the University of Pennsylvania was 58.4 years.

In our relatively small series of 24 patients with multiple primary malignant lesions of the large intestine, the average age was 63.3 years. In this group, the average age of the 16 patients with simultaneous lesions was 60.5 years (Table I), and the average age of the 8 patients with nonsimultaneous carcinomas was 64.8 years when the first carcinomas were found and 69 years when the second carcinomas were diagnosed.

The age recorded for the 8 patients with nonsimultaneous carcinomas, as shown in Table II, is the time when the second carcinoma was diagnosed.

While our figures do not agree insofar as age is concerned, the weight of evidence in the literature indicates that multiple carcinomas develop at the same age or slightly earlier than single carcinomas.

Duration of Symptoms. The symptoms of cancer of the large intestine are rather nonspecific and vague, and patients often disregard them until blood in the stools provokes immediate quest for medical aid.

Multiple simultaneous lesions might be expected to produce symptoms somewhat earlier than single lesions and actually this was true in this group of patients. The average duration of symptoms in patients with simultaneous lesions was 8.9 months, as

TABLE II

MULTIPLE NONSIMULTANEOUS PRIMARY CARCINOMAS OF THE COLON, HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA 1940–1951

Case	Sex	Age* yr.	Location of Lesion			Associated Polyps
			First carcinoma	Second carcinoma	Third carcinoma	
17. Y.B.	F	81	Transverse colon, April 1943	Sigmoid, June 1950	Cecum Feb. 1951	Yes
18. L.E.	F	68	Descending colon, June 1942	Transverse colon, June 1944		No
19. G.F.	M	50	Descending colon, March 1947	Transverse colon, rectum, Oct. 1950		Yes
20. M.K.	M	68	Sigmoid, Oct. 1950	Descending colon, Jan. 1952†		No
21. A.M.	F	62	Transverse colon, April 1945	Transverse colon, Jan. 1952†		Yes
22. T.P.	F	85	Sigmoid, May 1946	Cecum, June 1947		No
23. F.R.	F	74	Ascending colon, Nov. 1940	Sigmoid, Feb. 1949		No
24. W.Z.	M	64	Sigmoid, May 1949	Cecum, Jan. 1951‡		Not known

* Age at time of second carcinoma.
† It will be noted that second lesion was diagnosed in Jan. 1952.
‡ Verified surgically, but not pathologically, as the lesion was not resected.

compared to 10.2 months for the patients in the nonsimultaneous group who were having their first carcinoma. Other authors have found this to be true.[26]

It is interesting to note that individuals in the nonsimultaneous group have symptoms for a much shorter time when the second tumor is developing. These persons seem to become aware of their symptoms sooner as a result of their experience with the first cancer. In Case 19, there were multiple polyps and the patient continuted to have symptoms subsequent to removal of the original carcinoma. The patient in Case 24 had had symptoms for four months, but was found to have a recurrent carcinoma of the sigmoid as well as a new and independent malignant lesion in the cecum. The average duration of symptoms in 4 other patients of the nonsimultaneous group was only two months. The average elapsed time between the first and second carcinomas was four years. The shortest interval was thirteen months and the longest was eight years and three months. Cases 20 and 21 were asymptomatic when the second carcinomas were detected. Such cases illustrate the importance of follow-up examinations.

Some authorities[7] have expressed the opinion that certain people are born with or acquire a type of tissue that tends to undergo cell hyperplasia and malignant change more readily than do the tissues of others. They believe that a person who has had one cancer is more likely to develop a

Fig. 4. Case 7. Roentgenogram showing an annular carcinoma in the ascending colon. The pathologic specimen showed two carcinomas in the ascending colon.

second one than is an individual who has never had the disease. If this is true, patients who have had a resection of the intestine for carcinoma should be examined every six months to a year probably for the rest of their lives.

Diagnosis. Fourteen of the 16 patients with simultaneous carcinomas were operated upon and found to have thirty separate tumors. In each of 5 cases, one carcinoma was diagnosed preoperatively and one was missed. In a sixth case, one carcinoma was diagnosed preoperatively, a second was missed, and a third was suggested, but missed at operation. Summaries of these 6 cases are recorded in this report.

The *findings* in this series coincide with the impression gained by perusal of the literature. Lesions of the rectum and rectosigmoid are diagnosed in a high percentage of cases. Unfortunately, when cancers are found with the proctoscope or sigmoidoscope, often no attempt is made to examine the rest of the large intestine where a second carcinoma or precancerous polyp may be located. The importance of a complete examination of the colon by barium enema in these patients cannot be overemphasized. When, for any reason, the colon has not been examined by barium sulfate enema preoperatively, the roentgenologic examination must be carried out as soon after operation as is feasible.

When two malignant tumors are located in the same segment of the bowel, such as in Cases 7, 9, and 12, only one tumor may be found before operation. In these cases, however, because of proximity to the tumor which led to the operation, the additional tumors are usually found by the surgeon or pathologist; Figure 4 (Case 7) illustrates this point. The barium enema showed a carcinoma in the ascending colon (Fig. 4). The pathologist found two malignant lesions, the large one which was demonstrated roentgenographically and a second smaller one which was not demonstrated by the roentgen studies.

When the growths occur in different parts of the colon, the possibility of overlooking a second carcinoma either before or at operation is considerable, as shown in Figure 5 (Case 9). In this case, the barium sulfate enema demonstrated an obstructing lesion at the hepatic flexure (Fig. 5*A*). A second defect suggested the possibility of a

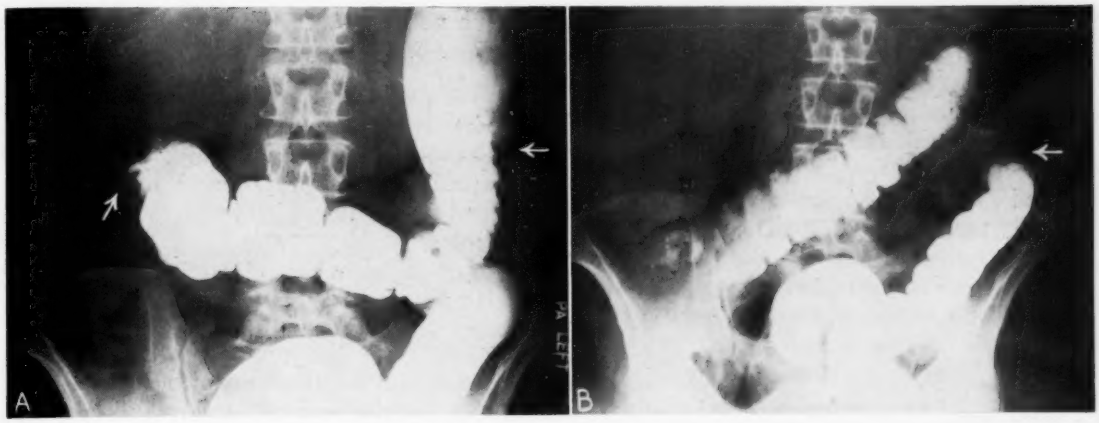

Fig. 5. Case 9. (*A*) May, 1947, carcinoma of the transverse colon. Also note short constricting defect in descending colon. At operation, two carcinomas were found in the transverse colon, but none in the descending colon. (*B*) January, 1948, definite annular lesion in descending colon.

second carcinoma in the descending colon. At operation, the large malignant lesion in the hepatic flexure was confirmed and a second polypoid carcinoma was found adjacent to it. In addition, several polyps were present in the same region. There was no evidence of metastasis to the regional nodes. Apparently, a lesion in the descending colon was overlooked. Six months later, the patient returned for routine re-examination and the barium enema (Fig. 5*B*) showed a definite annular carcinoma at the site of the original defect. The tumor was resected and this time there was metastasis to the regional lymph nodes.

The importance of a complete examination of the colon is apparent. It has often been customary in the past to omit the barium enema when a carcinoma of the rectum has been discovered by digital or proctoscopic examination. This procedure should be carried out, unless there is danger of acute intestinal obstruction. The entire colon should be examined as thoroughly as possible in all cases. Double contrast examinations should be performed in addition to the standard barium enema in all cases of carcinoma to detect additional tumors—either benign or malignant. When these procedures are contraindicated preoperatively, they should be completed postoperatively because multiple lesions may elude very careful palpation of the colon by the surgeon.

Summaries of Cases in Which Simultaneous Carcinomas Were Missed Preoperatively, Although One Carcinoma Was Diagnosed Preoperatively

Case 1. F.B., a sixty year old woman, admitted to the Surgical Service of the Hospital in September, 1945, complaining of rectal pain, constipation and diarrhea of three months' duration. There was a palpable mass in the left lower quadrant of the abdomen. Proctoscopic examination showed a rectal mass and several polyps. A barium enema was not done. Preoperative diagnosis: carcinoma of the rectum.

Examination of the resected specimen showed two carcinomas, one in the rectum and the other in the sigmoid; there were also associated polyps.

Case 2. S.B., a fifty-three year old man, admitted to the Surgical Service of the Hospital in November, 1941, because of rectal bleeding, first noted two years previously. Digital rectal examination revealed a mass. A barium enema was not done. Preoperative diagnosis: carcinoma of the rectum.

Examination of the resected specimen showed two carcinomas, one in the rectum and the second in the sigmoid. There were no associated polyps.

Case 7. B.G., a sixty-two year old woman, admitted to the Surgical Service of the Hospital in June, 1948, with intestinal obstruction. She had had abdominal pain for about six months. She complained of diarrhea and the loss of several pounds in weight. A barium enema performed elsewhere had shown an annular carcinoma in the ascending colon.

At operation, in addition to the constricting lesion, there was a smaller flat ulcerating tumor 5 cm. distal to the large carcinoma (Fig. 4). There were no associated polyps.

Case 9. S.J., a fifty-four year old woman, admitted to the Surgical Service of the Hospital in May, 1947, because of pain in the right abdomen of one year's duration. Occasional nausea and she had lost about 6 pounds in weight. No change in bowel habits, no rectal bleeding. Examination of the abdomen disclosed a firm, nodular, tender mass about 7 or 8 cm. in diameter in the right abdomen at about the level of the umbilicus. The barium enema revealed an annular lesion in the transverse colon, just distal to the hepatic flexure (Fig. 5*A*). The roentgenologist also called attention to a short constricted area in the descending colon just distal to the splenic flexure, which might represent a second lesion.

At operation, a mass about 6 cm. in diameter was found in the region of the hepatic flexure corresponding to the tumor demonstrated roentgenographically. Just proximal to the large carcinoma were several small pedunculated polyps. A few centimeters distal to the main lesion there was a single, large, friable, hemorrhagic polypoid lesion 5 by 2 by 2 cm. on a 2 cm. pedicle.

Microscopic sections from the two larger lesions showed carcinoma. The regional lymph nodes were not involved. An annular lesion in the region of the splenic flexure apparently was not found.

The patient recovered uneventfully and gained 20 pounds in weight.

She returned for routine re-examination in October, 1947, and a barium enema showed a definite annular neoplasm in the descending colon at the site of the previously noted defect. Patient would not consent to re-operation, but she returned in January, 1948, when the constricting lesion was again demonstrated (Fig. 5*B*). Operation was again advised and accepted.

An annular carcinoma was resected; several lymph nodes were found to contain metastatic carcinoma.

Case 12. L.P., a fifty-nine year old woman, admitted to the Surgical Service of the Hospital in December, 1947, complaining of abdominal pain of two weeks' duration. A barium enema showed a large fungating lesion in the descending colon.

At operation a second carcinoma about 2.5 cm. in diameter was noted adjacent to the large tumor. There were no associated polyps.

Case 13. A.S., a seventy-two year old man, admitted to the Surgical Service of the Hospital in October, 1947, because of abdominal pain and constipation of two months' duration. Proctoscopic examination was negative. A barium enema showed a long constricting lesion in the sigmoid extending into the descending colon.

At operation the large lesion was confirmed. In addition, a second carcinoma about 2 cm. in diameter was found in the rectosigmoid; it involved the entire thickness of the bowel wall. Several polyps were also present and one of these showed malignant transformation but no invasive qualities (it is not included as a separate carcinoma).

Distribution. When a series of cases of single carcinomas of the large intestine is analyzed, it is usually found that roughly 75 per cent of the lesions are located in the rectum, rectosigmoid and sigmoid, while the remaining 25 per cent are scattered throughout the other portions of the colon.

The distribution of 288 cases of single carcinomas of the colon and rectum[3] at the Hospital of the University of Pennsylvania is summarized in Table III.

The distribution of 34 simultaneous carcinomas in this series, also tabulated in Table III, is found to roughly parallel that of single lesions.

On the other hand, there is a striking difference in the location of 18 nonsimultaneous carcinomas, shown in Table III, in that 50 per cent of the tumors were in the cecum, ascending and transverse colon. Thomas and his co-workers[26] indicated that the difference is even more striking when the first of the nonsimultaneous carcinomas are analyzed. In their group, 50 per cent of

Table III

DISTRIBUTION OF SINGLE AND MULTIPLE CARCINOMAS OF THE COLON, HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

Location	Single Lesions*		Multiple Lesions			
			Simultaneous		Nonsimultaneous	
	No.	Per cent	No.	Per cent	No.	Per cent
Rectum, Rectosigmoid	136	47.2	10	29.4	1	5.6
Sigmoid	74	25.7	12	35.3	5	27.8
Descending colon	17	5.9	3	8.8	3	16.6
Transverse colon	12	4.2	5	14.7	5	27.8
Ascending colon, Cecum	49	17.0	4	11.8	4	22.2
Totals	288	100.0	34	100.0	18	100.0

* This group analyzed by Bender.[3]

the original lesions in patients who were destined to later develop a second carcinoma were in the ascending colon. That was not the case in this series (see Table II), nor in a small group of asynchronous carcinomas reported by Rankin and Conger.[23] The reason for the difference in distribution between simultaneous and nonsimultaneous carcinomas is not apparent.

Relationship of Adenomatous Polyps to Cancer of the Large Intestine. Polyps of the colon and rectum are definitely precancerous, and numerous studies have shown that a high percentage, if not the majority of carcinomas, arise in adenomatous polyps.[6,11,16,17,23,28]

The following case illustrates the importance of polyps in the development of carcinoma of the large intestine:

Case 21. A.M., a fifty-six year old woman, admitted to the Surgical Service of the Hospital in April, 1945, complaining of abdominal pain. She was well until December, 1943, when she first had an attack of cramp-like abdominal pain followed by nausea and vomiting. At first the attacks occurred at monthly intervals, but gradually increased in frequency until they took place every two to three days. She had been constipated as long as she could remember. She had lost about 25 pounds since the onset of symptoms. Physical examination revealed an epigastric mass extending almost to the level of the umbilicus. A barium enema showed an annular lesion in the distal portion of the transverse colon (Fig. 6*A* and *B*).

Segmental resection was carried out and she remained symptom-free.

Patient returned for a routine re-examination in 1949, and the roentgenologic examination of the colon was interpreted as negative. However, a review of the films made at that time showed a definite polypoid lesion in the proximal portion of the transverse colon (Fig. 6*C*). She was not seen again until January, 1952, when she returned for another re-examination. She had no complaints. The barium enema showed a long annular carcinoma in the transverse colon just distal to the hepatic flexure (Fig. 6*D*).

Segmental resection was done and no polyps were found in the resected part of the colon. However, postoperative double contrast films showed at least two small polyps in the descending colon.

Routine proctoscopic examination shows that about 8 per cent of individuals having no gastrointestinal complaints have colonic polyps.[11,15] The incidence would undoubtedly be higher were results of roentgen examinations included. DeMuth, Cherney and Fitts[11] reviewed 234 cases of polyps of the large intestine encountered in the Surgical Clinic of the Hospital of the University of Pennsylvania during the years 1943 to 1951. The average age was fifty-five years. Fifteen per cent of the lesions had undergone malignant transformation. In 33 per cent of the individuals who had polyps, more than one was present and in 18 per cent more than two polyps were found.

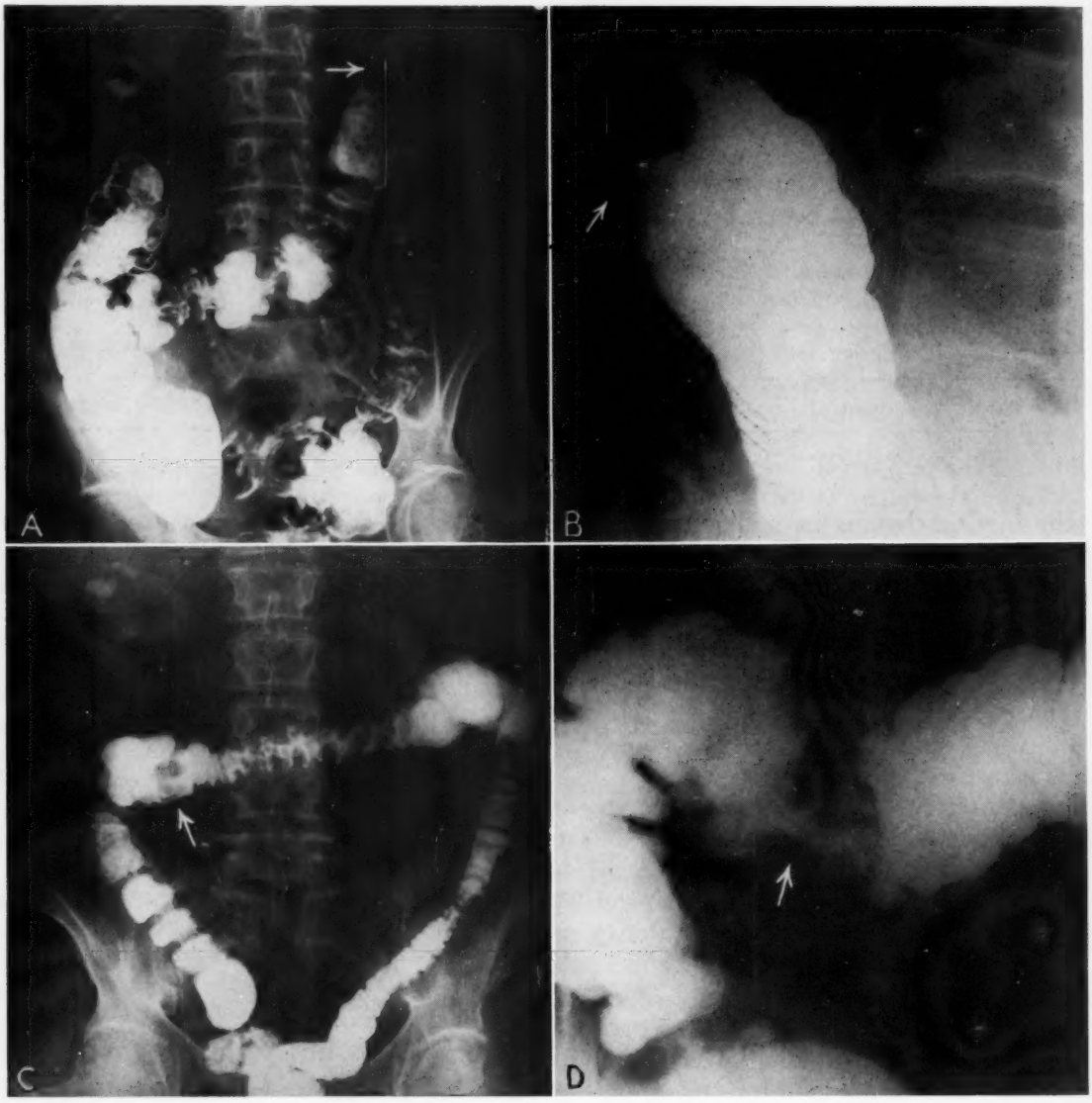

FIG. 6. Case 21. (*A*) April, 1945, carcinoma of the transverse colon at splenic flexure. (*B*) Spot film of lesion shown in (*A*). (*C*) 1949, polypoid defect in proximal portion of the transverse colon. (*D*) January, 1952, annular carcinoma at site of defect, noted in (*C*).

Polyps of the colon and rectum are present more often in patients who have a carcinoma of the bowel than in patients in whom no carcinoma is found. In our experience, 20 per cent of 175 patients with single carcinomas, whose records were reviewed, had associated polyps. In the group with multiple primary carcinomas, associated polyps were present in 10 of 21 patients who underwent resection—an incidence of almost 50 per cent.

Various excellent roentgenologic procedures and techniques have been devised to demonstrate polyps of the large intestine.[10,20,21,25,29] Discussion of these methods is not within the scope of this report.

SUMMARY AND CONCLUSIONS

Multiple primary carcinomas of the colon and rectum are not rare, and it has been shown by previous investigators that the incidence is greater than would be

expected on the basis of chance alone. The incidence is probably greater than present statistics indicate, because many so-called recurrent carcinomas very likely are actually new and independent tumors.

Review of the literature indicates that the occurrence of multiple carcinomas is probably not closely linked with senescence, but that some individuals have tissues that are predisposed to the development of cancer. According to some observers, an individual who has had one malignant tumor is more likely to develop a second lesion that a patient who has never had malignant disease.

There is an interesting difference in distribution of multiple nonsimultaneous as compared to simultaneous carcinomas. The distribution of simultaneous carcinomas roughly parallels that of single carcinomas; about 75 per cent of the lesions are in the rectum and sigmoid, while the remaining 25 per cent are scattered throughout the other segments of the colon. On the other hand, 50 per cent of the nonsimultaneous carcinomas are located in the cecum, ascending and transverse colon. The reasons for these findings are not apparent.

The incidence of associated adenomatous polyps is even greater with multiple carcinomas than it is with single carcinomas of the large intestine.

Discovery of one carcinoma should lead to a complete examination of the entire colon. Often in the past, it has been customary to omit the barium enema when proctoscopy revealed a malignant tumor in the rectum. This diagnostic procedure should be performed, unless there is danger of acute intestinal obstruction. Double contrast examination should be made, in addition to the standard barium enema, in all cases of cancer of the large intestine in order to detect additional tumors—either benign or malignant. In many cases, these procedures cannot be carried out preoperatively, but should be performed postoperatively because multiple tumors may escape careful palpation of the colon by the surgeon.

All patients who have had resection of the colon for carcinoma should be followed up at intervals of six months to a year, probably for the rest of their lives, so that new lesions can be detected before the onset of symptoms. Recurrence of symptoms should not necessarily be considered as evidence of return of the primary lesion, because a new and independent growth may be present even in the region of the anastomotic site of a previously removed cancer. The prognosis of new lesions is far better than that of recurrent malignant tumors.

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The author wishes to express his indebtedness to Dr. Eugene P. Pendergrass and Dr. Philip J. Hodes for their invaluable advice in the preparation of the manuscript, to Dr. Robert C. Horn, Jr. for reviewing the pathology slides, to Dr. I. S. Ravdin for permission to use the surgical records and to Dr. W. T. Fitts, Jr. for the use of some of his data on polyps of the colon and rectum.

REFERENCES

1. BACON, H. E., and TAVENNER, M. C. Multiple primary malignant tumors involving colon and rectum; report of 94 cases. *Am. J. Surg.*, 1952, *83*, 55–63.
2. BARGEN, J. A., and RANKIN, F. W. Multiple carcinomata of large intestine. *Ann. Surg.*, *91*, 583–593.
3. BENDER, D. H. Cited by DeMuth, Cherney and Fitts.[11]
4. BERSON, H. L., and BERGER, L. Multiple carcinomas of large intestine. *Surg., Gynec. & Obst.*, 1945, *80*, 75–84.
5. BILLROTH, C. A. T. Quoted by Warren and Gates.[27]
6. BINKLEY, G. E., SUNDERLAND, D. A., MILLER, C. J., STEARNS, M., and DEDDISH, M. R. Carcinoma arising in adenomas of colon and rectum. *J.A.M.A.*, 1952, *148*, 1465–1469.
7. BRINDLEY, G. V. Multiple primary malignancies of large intestine. *South .M. J.*, 1938, *31*, 355–362.
8. BUGHER, J. C. Probability of chance occurrence of multiple malignant neoplasms. *Am. J. Cancer*, 1934, *21*, 809–824.
9. BURKE, M. Multiple primary cancers. *Am. J. Cancer*, 1936, *27*, 316–325.

10. CHRISTIE, A. C., COE, F. O., HAMPTON, A. O., and WYATT, G. M. Value of tannic acid enema and post-evacuation roentgenograms in examination of colon. AM. J. ROENTGENOL. & RAD. THERAPY, 1950, *63*, 657–663.
11. DEMUTH, W. E., JR., CHERNEY, P. J., and FITTS, W. T., JR. Adenomatous polyps of colon and rectum; a challenge in cancer prophylaxis. *Surg., Gynec. & Obst.*, 1952, 94, 195–199.
12. DORN, H. F. Quoted by DeMuth, Cherney, and Fitts.[11]
13. EWING, J. Neoplastic Diseases. Third edition. W. B. Saunders Company, Philadelphia, 1928.
14. HANLON, F. R. Multiple primary carcinomas. *Am. J. Cancer*, 1931, *15*, 2001–2012.
15. HAUCH, E. W., BUIE, L. A., BARGEN, J. A., and SMITH, L. A. Adenoma of rectum and sigmoid colon: incidence revealed by proctosigmoidoscopic examination of group of patients free of complaints referable to colon and rectum. *Gastroenterology*, 1950, *16*, 669–673.
16. LAURENS, J., and BACON, H. E. Relationship of adenomatous polyps to malignancy. (In press.) Quoted by Bacon and Tavenner.[1]
17. LOCKHART-MUMMERY, J. P., and DUKES, C. Precancerous changes in rectum and colon. *Surg., Gynec. & Obst.*, 1928, *46*, 591–596.
18. LONG, J. W., MAYO, C. W., DOCKERTY, M. B., and JUDD, E. S., JR. Recurrent versus new and independent carcinomas of colon and rectum. *Proc. Staff Meet., Mayo Clin.*, 1950, *25*, 169–178.
18a. MARSHAK, R. H. Multiple carcinomas of the large bowel. *Radiology*, 1950, *54*, 729–731.
19. MIDER, G. B. Multiple invasive carcinomas of large intestine. *Surgery*, 1946, *20*, 744–748.
20. MORETON, R. D., STEVENSON, C. A., and YATES, C. W. Fictitious polyps as seen in double-contrast studies of colon. *Radiology*, 1949, *53*, 386–393.
21. MORETON, R. D., COOPER, E. M., and FOEGELLE E. F. Simple one-stage method of double-contrast study of colon. *Radiology*, 1951, *56*, 214–221.
22. OLSSON, O. Cancer coli multiplex. *Acta radiol.*, 1945, *26*, 415–424.
23. RANKIN, F. W., and CONGER, A. B., JR. Metachronous carcinomas of colon. *J.A.M.A.*, 1951, *146*, 918–920.
24. SHEINFELD, W. Synchronous colon carcinomas of multicentric origin. *New York State J. Med.*, 1948, *48*, 85–87.
25. TEMPLETON, F. E., and ADDINGTON, E. A. Roentgenologic examination of colon using drainage and negative pressure; with special reference to early diagnosis of neoplasm. *J.A.M.A.*, 1951, *145*, 702–704.
26. THOMAS, J. F., DOCKERTY, M. B., and WAUGH, J. M. Multiple primary carcinomas of large intestine. *Cancer*, 1948, *1*, 564–573.
27. WARREN, S., and GATES, OLIVE. Multiple primary malignant tumors; survey of literature and statistical study. *Am. J. Cancer*, 1932, *16*, 1358–1414.
28. WEBER, H. M. Diagnosis of early intestinal cancer. AM. J. ROENTGENOL. & RAD. THERAPY, 1950, *64*, 929–937.
29. WEBER, H. M. Roentgenologic demonstration of polypoid lesions and polyposis of large intestine. AM. J. ROENTGENOL. & RAD. THERAPY, 1931, *25*, 577–589.

DISCUSSION

DR. ROBERT D. MORETON, Fort Worth, Texas. Dr. Tondreau has made a very fine presentation. He has reminded us that multiple primary malignant tumors of the colon are not rare and has given an excellent review of the literature.

The inherent susceptibility to cancer that Thomas, Dockerty and Waugh concluded were present in some individuals accounting for the occurrence of multiple malignant neoplasms seems to be nothing more than the intrinsic factor which Liljencrantz felt was inherent in the germ plasm of the individual and would be an etiologic factor in consideration of any cancer.

A very excellent series of cases has been added to the literature with this presentation. The finding of carcinomas in asymptomatic individuals should make us more alert to pick up the very small polyps and I feel any type examination suitable to do this should be a routine procedure. I personally prefer the double contrast method but certainly do not feel that it is the only examination which is satisfactory for this purpose. Gianturco has done an excellent job using high voltage roentgenographic studies of the colon. Certainly in his hands the method is most accurate in demonstrating 24 polyps in 650 colons examined. Only 10 of 24 patients had noticed rectal bleeding. Also the semitransparent enema used by Potter and others is most effective in their hands. I therefore feel that the individual radiologist should employ the method he can use most accurately and use it if possible routinely to discover these small lesions which may be primary or associated with the larger more obvious one which caused the patient to seek the doctor.

In Dr. Tondreau's series, Cases 1 and 2 did not have roentgen examination of the colon before surgery. I think we all agree that such an examination should be a "must" in all patients

who are to receive an adequate examination and proper surgery.

Also the two patients whose films were re-studied and it was found that their cancers were not detected the first time reminds us that we should examine each patient and his films as if we ourselves were being examined. In spite of a normal fluoroscopic examination and normal appearance at the initial inspection occasionally the final check will reveal a small lesion or area of questionable pathology in the bowel. These persons should at least be re-examined after further preparation and particular attention paid to that area. We are all going to miss some, but such a procedure will keep these at a minimum.

Lastly, I agree completely with the conclusions reached and thank Dr. Tondreau for bringing us this excellent paper.

ANTERIOR SACRAL MENINGOCELE*

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THE purpose of this communication is to add 4 cases of anterior sacral meningocele to the small group already published. These are previously unreported cases.

Recent articles[3,4,6] have discussed the clinical findings in this rare condition, and it would be repetitious to enumerate them here. We would, however, like to emphasize the importance of recognition of this condition in women who are still in the childbearing period, and who may develop serious complications during labor; this may occur through rupture of the meningocele, through mechanical obstruction of the outlet, and through increased intraspinal and intracranial pressure by compression of the cyst.

Our own experience convinces us that this entity is not generally known among physicians. Prior to the advent of roentgenology, the diagnosis was rarely made during life, and became known only through postmortem examination. Today, the radiologist can recognize the condition instantly on films of the sacrum and coccyx, by the characteristic deformity of these structures produced by growth of the meningocele. Since the radiologist usually is first to make the diagnosis (as in 3 of our 4 cases) he assumes an important role in the case—that of familiarizing the referring physician with the entity and of its potential dangers if not properly handled. Sherman *et al.*[6] discuss the high mortality from meningitis in those patients who underwent surgical removal of the cyst, or aspiration of the cyst through the rectum or vagina, in the pre-antibiotic drug era. Fortunately, most postoperative complications can be prevented or successfully treated today.

CASE REPORTS

CASE 1. J.B., an eighteen year old white female college student. In March, 1950, the patient first noted intermittent pain in the lower end of her spine. By August, the pain was worse. Roentgenograms made in October showed a "forked coccyx." The patient was treated with sitz baths, but obtained no relief. In January, 1951, a rectal examination revealed a mass between the rectal wall and the coccyx. The pain had continued to grow worse, particularly after sitting for any length of time. She went to Johns Hopkins Hospital for diagnosis; the opinion given by the examining doctor was as follows: "Tumor of congenital origin, congenital defect of the spine such as spina bifida with an anterior meningocele."

Roentgenograms made there were reported as showing "a congenital anomaly of the lower end of the sacrum and coccyx with a widening and failure of fusion in the midline." Surgery

FIG. 1. Case 1. A midline deformity of the lower sacrum is present. The coccyx lies to the left of the midline. The soft tissue shadow of the large meningocele is visible, filling the greater portion of the pelvis.

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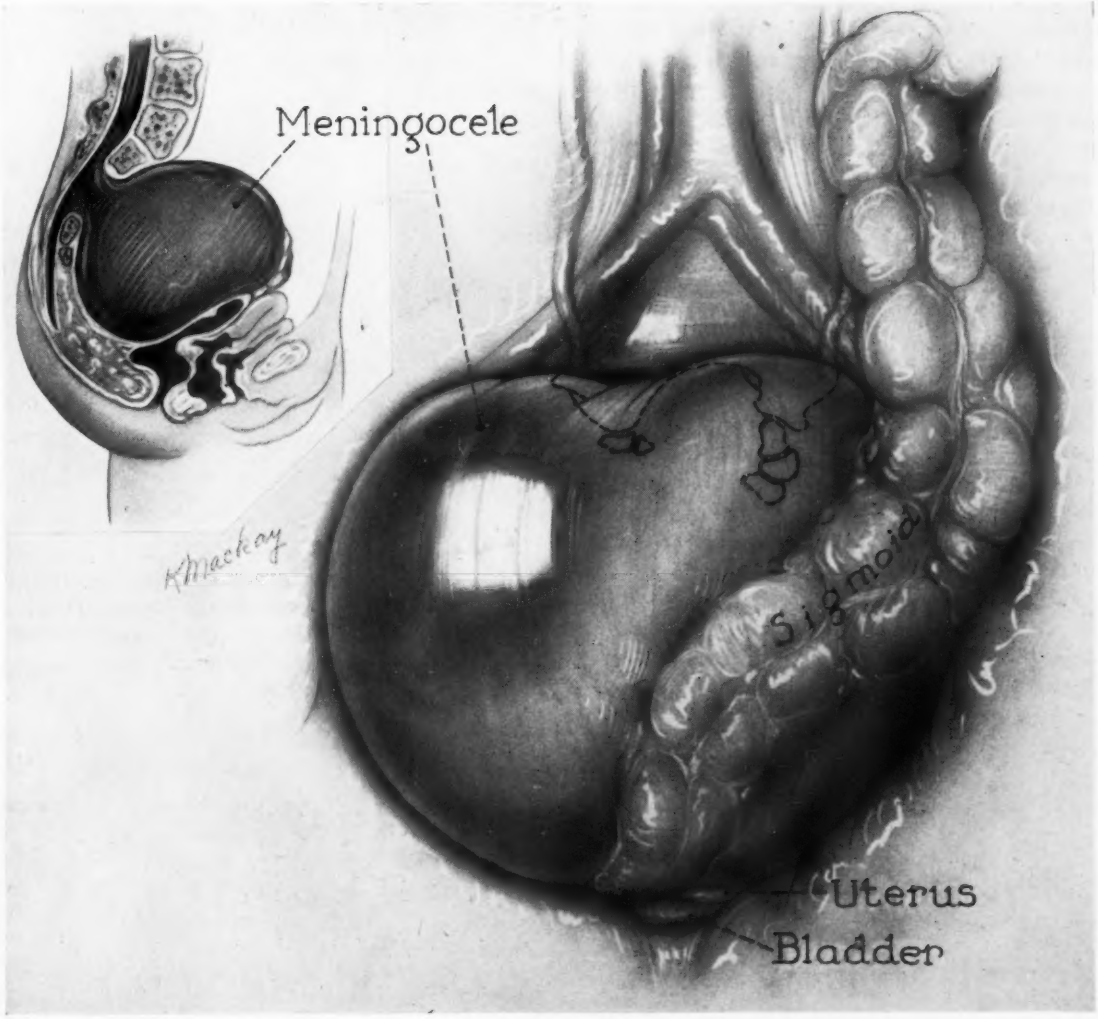

Fig. 2. Case 1. Drawing of meningocele in situ as seen at surgery. The relationship of the meningocele to the bladder, uterus, colon, and ureters is depicted. The deformed portion of the sacrum is outlined in dotted lines at the superior aspect of the cyst. Insert depicts the relationship of the meningocele and its pedicle entering the spinal canal.

was advised, but since the patient wished to be nearer her home, she was admitted to Emory University Hospital on March 20, 1951.

Her past history revealed chronic constipation, recurrent pyelitis until eight years of age, and an appendectomy for chronic appendicitis "several years ago."

Physical examination was essentially normal except for the rectal examination; this revealed a large mass outside the posterior wall of the rectum, smooth and cystic, nontender, and without surrounding induration. Palpation of the sacrum posteriorly revealed a median defect.

Laboratory examinations were noncontributory. Roentgenograms of the abdomen made following admission again showed the sacral and coccygeal deformity, characteristic of anterior sacral meningocele (Fig. 1).

Operation was done, and the report was as follows: "Immediately after division of this dense fascial layer, there herniated into the wound a thin-walled cystic structure which transmitted a bluish color (Fig. 2). By blunt and sharp dissection the cyst was freed from the bifid region of the sacral spine and laterally from within the pelvis. The rectum lay anterior to the cyst and this stripped off with some diffi-

culty. During this portion of the procedure the cyst was entered, and found to contain water-clear fluid. The inner wall was perfectly smooth and glistening, and the entire cystic structure appeared to be suspended from a 0.5 cm. pedicle, lying within the sacral canal. On inspection of this area there appeared to be seepage of spinal fluid from above downward. No nerve trunks were visualized during the dissection." The cyst was removed and its pedicle was ligated.

The patient made an uneventful recovery, and was relieved of her symptoms by the removal of the cyst.

Case II. V.P.W., a forty-eight year old white female, married. In August, 1948, the patient was seen by her gynecologist for a routine check-up. She states that some kind of tumor was found in the pelvis. She denies any symptoms from this tumor.

Past history revealed rheumatoid arthritis at the age of twenty-seven, with residual weakness of legs and stiffness of hips. Appendectomy "years ago."

Fig. 3. Case II. Detail of the pelvic region from an excretory urogram. A scythe-shaped deformity of the lower sacrum and coccyx is present. Double ureters are present on the right. A single ureter was present on the left side. The soft tissue shadow of the meningocele is visible.

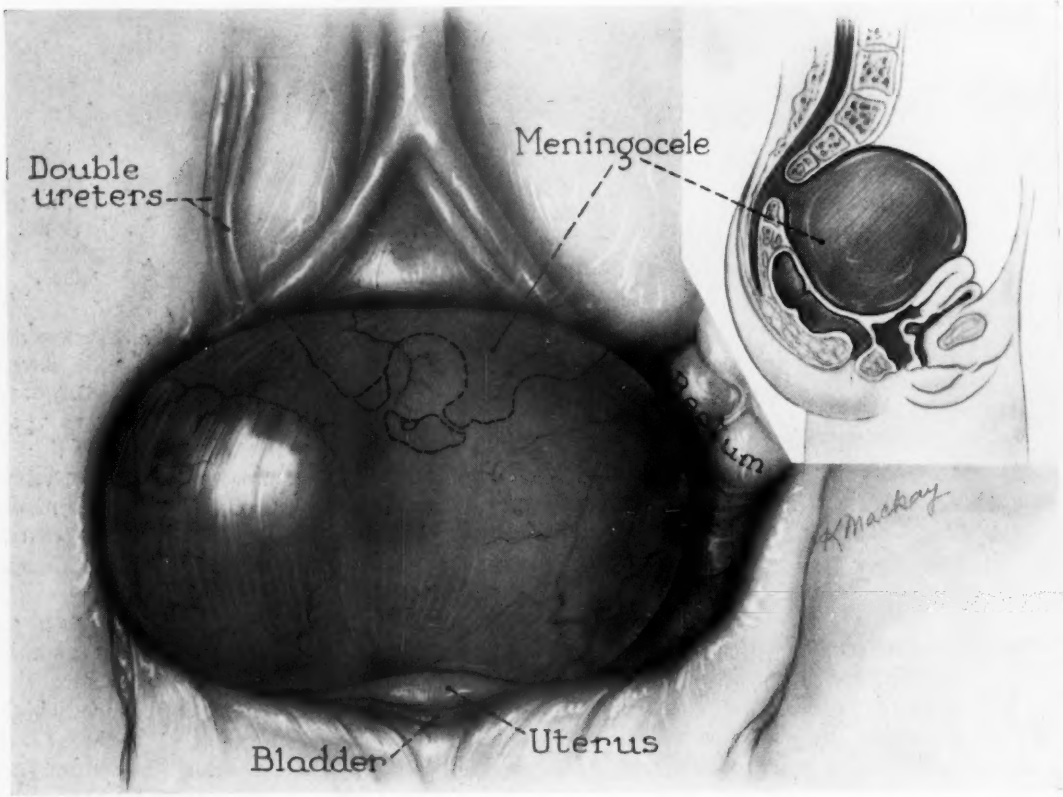

Fig. 4. Case II. Drawing of meningocele as seen at surgery. Its relationships with surrounding structures are depicted in the two views. The double ureters on the right are seen. The deformed sacrum and coccyx are shown as dotted lines at the top of the meningocele. The stalk is visible in the insert.

Fig. 5. Case III. Anteroposterior view of the sacrum and coccyx, showing the characteristic sickle shape deformity.

Physical examination was essentially negative except for the vaginal and rectal examinations; a cystic mass could be felt occupying the pelvic region; this was nontender.

Excretory urograms revealed double ureters and double kidneys bilaterally, and compression of the urinary bladder superiorly. There was a deformity of the sacrum and coccyx, characteristic of anterior sacral meningocele (Fig. 3).

Operation was performed on November 24, 1948. On exploration of the pelvic region, a large retroperitoneal cyst was found which extended backward into the cul-de-sac and sacrum (Fig. 4). The cyst measured approximately 8 by 15 cm. in size. The peritoneum was opened vertically, the double ureters on the right were retracted laterally and the cyst broken into, yielding clear, yellowish fluid. The sac of the cyst was dissected free without injury to the major vessels or nerves. The sac originated "at, near, or in the sacrum." A small dimple was found at the point of origin. The entire wall of the cyst was excised.

Microscopically, the cyst wall contained a large amount of fibrous connective tissue, and an abundant amount of muscle tissue. There were nerves present in the wall, which were made up of myelinated fibers.

Shortly after operation, the temperature suddenly rose to 102° F. Between the first postoperative day and December 9 (fourteen days), the patient received 6,500,000 units of penicillin. During this time, the temperature gradually returned to normal. There was difficulty in voiding for several days after the operation. There were no clinical findings of meningitis at any time.

She was discharged from the hospital on December 24, 1948.

Case III. R.S., a forty-five year old white female, married. The patient was admitted to Crawford Long Hospital in Atlanta on December 29, 1951, with a diagnosis of acute cystitis. For four months she had had burning and pain on urination, and frequency of urination. She complained of nervousness, and frequent sickness at the stomach, which was not related to meals.

Physical examination was noncontributory. The vaginal and rectal examinations were not recorded.

Retrograde pyelograms revealed a deformity of the sacrum and coccyx characteristic of anterior sacral meningocele (Fig. 5). The kidneys and ureters appeared normal on these films; the bladder was not well outlined.

Films of the pelvic region made following instillation of a small amount of contrast medium into the lumbar subarachnoid space showed a deformed sacral sac, and several small

Fig. 6. Case III. Myelogram. The caudal sac is deformed. Small droplets of the contrast medium can be seen within the meningocele in the right pelvic cavity. Myelography is useful as confirmatory evidence of the presence of a meningocele.

Fig. 7. Case iv. Anteroposterior view of pelvic region showing a characteristic deformity of the lower sacrum and coccyx. The borders of the meningocele are not visible, but apparently it lies in the left pelvic cavity, where there is a significant lack of air-filled intestinal shadows.

flecks of contrast medium within the cyst (Fig. 6). A repeat film of the pelvic region several days later showed no further passage of the contrast medium into the cyst.

Urinalysis revealed numerous pus cells in the urine.

No further investigation was made.

Case iv. B.M.G., a twenty-two year old white female, married. In July, 1950, the patient was admitted to Emory University Hospital with the chief complaint of "bladder trouble." She frequently had bouts of urinary frequency, fever, and pain at the end of urination. There were no symptoms referable to the back.

Physical examination was essentially negative. Rectal and vaginal examinations were not recorded.

Cystoscopic examination showed three or four small polyps in the vesical outlet. The bladder was otherwise normal. Roentgenograms made during retrograde pyelography showed a deformity of the sacrum and coccyx having the characteristic appearance of an anterior sacral meningocele (Fig. 7).

No further investigation was made.

SUMMARY

1. Four cases of anterior sacral meningocele are reported in detail. Two of these patients were submitted to surgery, and the operative findings are described; one patient showed contrast medium in the meningocele following its instillation into the subarachnoid space in the lumbar region; the fourth patient was diagnosed by pelvic roentgenograms only.

2. Brief mention is made of the importance of accurate diagnosis, particularly when surgery is contemplated, and during pregnancy.

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We are indebted to Dr. Kells Boland, Jr., Dr. Richard Elmer, and Dr. Dudley King, for the use of Case iii in this series.

REFERENCES

1. Archer, V. W., Cooper, G., Jr., and Cimmino, C. V. Occult meningocele of sacrum. *Radiology*, 1948, *51*, 691–695.
2. Brown, M. H., and Powell, L. D. Anterior sacral meningocele. *J. Neurosurg.*, 1945, *2*, 535–538.
3. Calihan, R. J. Anterior sacral meningocele. *Radiology*, 1952, *58*, 104–108.
4. Eder, D. Anterior sacral meningocele. *Bull. Los Angeles Neurol. Soc.*, 1949, *14*, 104–112.
5. Ericsson, N. O. Ventral sacral meningocele. *Nord. med.* (*Hygiea*), 1945, *27*, 1465–1468.
6. Sherman, R. M., Caylor, H. D., and Long, L. Anterior sacral meningocele. *Am. J. Surg.*, 1950, *79*, 743–747.

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ROENTGEN THERAPY FOR CANCER OF THE LARYNX AND LARYNGOPHARYNX*

TWENTY YEARS' EXPERIENCE

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SINCE 1931 it has been the policy of the Laryngological Service of the Mount Sinai Hospital in New York City to refer practically all cases of cancer of the larynx and laryngopharynx for roentgen therapy. From 1931 to 1951, 220 cases have been treated with roentgen radiation as the method of choice. These cases include not only those on the Laryngological Service of the hospital but also patients referred from the private practices of laryngologists, mainly staff members of our hospital. The material presented in this article represents our personal experience in the use of roentgen therapy for cancer of the larynx and laryngopharynx.

CLASSIFICATION

Classification of these cases is essential to a proper understanding of the disease and the effects of treatment. It is unfortunate that at the present time there is no international method of classification of cancer of the larynx and laryngopharynx. Therefore we have followed an anatomical and surgical method which appears to us to be most useful in the analysis of treatment results. There is first a major division of the anatomical structures concerned into the intrinsic larynx and the extrinsic larynx. The intrinsic larynx, or the larynx proper, includes the vocal cords, the anterior commissure, the subglottic region, and the ventricle up to the free margin of the false cords. The extrinsic larynx, or laryngopharynx, includes those structures immediately above, lateral, and posterior to the intrinsic larynx, from the tip of the epiglottis to the cricoid cartilage. For purposes of study, cancer of the intrinsic larynx may be subdivided, according to surgical indications, into two groups: those suitable for surgical cure by cordectomy through a laryngofissure, and those which would require laryngectomy. Cancer of the extrinsic larynx or laryngopharynx may best be studied by a regional subdivision into anterior and posterolateral locations. The anterior location includes those lesions which are found on the epiglottis or false cord. The posterolateral location includes the aryepiglottic fold, the arytenoid, the pyriform sinus and the postcricoid lesions. A third subdivision of the laryngopharynx must also be made for those extensive lesions which occupy both anterior and posterolateral locations. Where both the intrinsic and extrinsic larynx are involved by cancer, the case is placed in the category of that location of the extrinsic larynx affected by the disease. With this method of classification we found useful significant differences in prognosis for the various groups.

Of the 220 cases treated primarily by roentgen irradiation from 1931 to 1951 (Table 1), the disease was limited to the intrinsic larynx in 117, while in 103 it was located in the laryngopharynx. In the intrinsic group, there were 31 cases which were originally suitable for cordectomy by laryngofissure, and 86 cases which would have required laryngectomy, had they been treated surgically. In the extrinsic group, the tumor was limited to the anterior section of the laryngopharynx, *i.e.*, the epiglottis and false cord, in 46 cases, while in 35 it was confined to the posterolateral section, including the aryepiglottic fold, arytenoid, pyriform sinus, and postcricoid

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TABLE I

CANCER OF THE LARYNX AND LARYNGOPHARYNX TREATED BY ROENTGEN IRRADIATION, 1931–1951

Total number of cases treated		220
Intrinsic		117
Originally suitable for cordectomy (laryngofissure)	31	
Originally would require laryngectomy	86	
Extrinsic (laryngopharynx)		103
Anterior lesions (epiglottis, false cord)	46	
Posterolateral lesions (arytenoid, aryepiglottic fold, pyriform sinus, postcricoid)	35	
Extensive lesions (both anterior and posterolateral locations)	22	

region. In the remaining 22 cases, the tumor was extensive and involved both the anterior and posterolateral locations.

AGE INCIDENCE

A study of the age incidence (Chart 1) in our series of cases shows that the ages

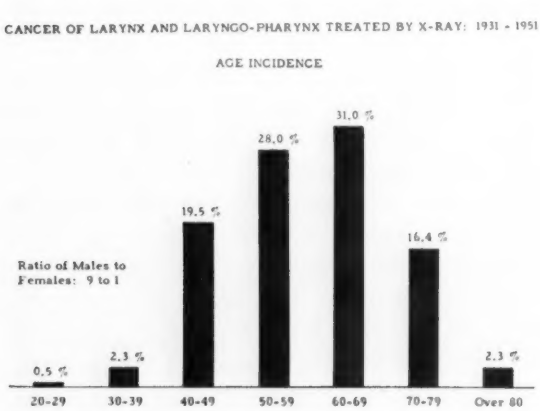

CHART 1

between fifty and sixty-nine years acount for three-fifths of all the cases. However, the incidence in patients who are over seventy years of age is almost 20 per cent. On the other hand, cancer of the larynx and laryngopharynx is uncommon betweeen the ages of thirty and thirty-nine years and rare at any younger age. The ratio of males to females is 9 to 1.

CASE STUDY

A detailed original status of the exact extent of the disease is made in every case by the laryngologist and the radiotherapist so that the case may be properly classified and evaluated for treatment. Roentgenographic studies of the neck, including laminagraphy, are also made. A positive biopsy was obtained in every case treated. In all except 2 cases, the histopathological report was squamous cell carcinoma. In the 2 exceptions, it was adenocarcinoma. No attempt was made to grade these tumors, not only because of the unreliability of this method, but also because of a previous demonstration by Harris and Klemperer[7] that the histopathological grade is of no prognostic value.

RADIATION TREATMENT

From 1931 to June, 1947, the period of time which includes all cases available for five year study, the technical factors of treatment have been more or less constant. The radiation employed was generated at 200 kv. peak and filtered by a Thoraeus filter. The half-value layer was 1.9 mm. Cu. The focal skin distance was 60 cm. The larynx and laryngopharynx were irradiated through two lateral, directly opposing, neck fields. The field size varied from 20 to 70 sq. cm., depending upon the extent and location of the tumor to be irradiated. A tumor dose of 4,700 to 6,000 roentgens, estimated in the center of the larynx, was delivered in twenty-eight to forty days. Such a dose required 3,600 to 4,500 r (measured in air) to each side of the neck, administered in daily fractions of 250 to 300 r (air). The r flux was 4 r per minute until 1938. After 1938, it was 12 r per minute. Beginning in July, 1947, we gradually altered our technique by employing higher kilovoltage, longer protraction, and greater total doses. In this more recent period we have treated 34 patients with 400 kv. radiation (half-value layer 3.5 mm. Cu) and 47 patients with 200 kv. roentgen rays (half-value layer 1.9 mm. Cu). With a

few exceptions, the over-all treatment time has been increased to six or seven weeks, or longer. While the daily tumor dose has been decreased to about 150 r, the total tumor dose has been increased to over 6,000 r. This tumor dose necessitates an increase in the dose to each field to over 4,000 r, in some cases to 5,000 or 6,000 r. Not enough time has elapsed for the proper evaluation of these changes in technique but we have observed that the reactions are less severe in spite of the greater doses employed.

The patients are treated in either a sitting or recumbent position. In general, the recumbent position is favored but the choice depends upon the cooperation and comfort of the patient. The size of the treatment portal is determined by the extent of the disease, and it is checked by roentgenograms taken with the therapy apparatus in treatment position. The positioning of the patient is important and it is done only by the radiotherapist at each treatment. Positioning during each treatment is checked by constant observation and by frequent interruptions for closer inspection. Restless patients, those with respiratory difficulties or cough, and those who are constantly clearing their throats or swallowing, require special methods of immobilization which include the use of treatment cones, sandbags and sedative medication. It is possible that a relatively slight movement on the part of the patient may cause a serious shift of the larynx out of the treatment field, which, if not recognized and corrected, may lead to failure. Constant vigilance on the part of the radiotherapist is an essential factor in the technique of treatment.

Since the patient is positioned by the radiotherapist, he is examined and observed daily. Frequent laryngeal examinations are performed by both the laryngologist and the radiotherapist for observation of the reactions and the airway. If the airway is dangerously narrow, the initial treatment may be administered very slowly in small doses together with antibiotic medication. In this manner, it may be possible to improve the airway by reduction of the swelling, if the laryngeal obstruction is due, in part, to inflammation. If tracheotomy is performed before or during the course of therapy, a tracheotomy tube made of plastic material is inserted during the actual treatment, since the silver of the ordinary tracheotomy tube may block part of the roentgen-ray beam directed to the tumor, especially in the region of the flange of the tube. There is also the theoretical objection that secondary radiation from the silver may cause local necrosis.

Supportive therapy is administered, as indicated, in the form of diet, fluids, vitamins, antibiotic drugs, sedative medication and hospitalization, if necessary, for intravenous fluids or blood transfusions.

Membrane reactions in the larynx are more likely to be observed in those cases treated within four weeks than in those in which the treatment is protracted. Erythema of the treated area of the skin usually appears about the third week and may become quite intense, with moist desquamation, if the over-all treatment period is short. In the protracted course, the skin undergoes a dry desquamation, which is usually healed by the sixth or seventh week. The skin reactions require no treatment except protection from clothes and direct sunlight.

After the course of therapy is completed, the patient is observed by the radiologist at frequent intervals together with the laryngologist. The immediate post-therapy period is a critical time for the observation of persistent or recurrent disease. In the successfully treated case, the disease usually disappears at the end of the course of therapy. Usually, an interval of one month is allowed for complete subsidence of the roentgen-ray reaction before laryngeal biopsy is taken if such is indicated. Follow-up examinations are performed at monthly intervals for the first two or three years. After that period the incidence of recurrence is relatively low, and the examination intervals may safely be lengthened.

Recurrent disease is best treated surgically, the type of operation, whether laryngofissure, partial laryngectomy, or total laryngectomy, depending upon the extent of disease found. Occasionally, re-treatment with roentgen radiation has been successful. Involved lymph nodes may be treated either surgically if operable or by irradiation if they are in the treatment field. If disease persists in the larynx, a combined laryngectomy and neck dissection may be performed.

FIVE YEAR RESULTS OF TREATMENT

The five year results of treatment were studied on the basis of all cases treated from 1931 to June, 1947. During this period of time, 139 patients with cancer of the larynx and laryngopharynx were treated with roentgen irradiation as the method of choice (Table II). This number does not include cases treated postoperatively. Of the total number treated primarily by roentgen irradiation, 114 were followed. An estimation of the cure rate for the entire clinical material is not of much value because cancer of the larynx and laryngopharynx represents a group of diseases rather than one disease, as indicated in our method of classification. However, for the sake of comparison with the results of some authors who reported their cure rates on the basis of all cases without classification, we made a similar computation. At the end of five years there were 67 cases alive and free of disease. On the basis of the determinate cases, this number represents an over-all five year cure rate of 59 per cent. If the indeterminate cases are considered as failures, the absolute five year cure rate is 48 per cent.

TABLE II

CANCER OF LARYNX AND LARYNGOPHARYNX, 1931–JUNE, 1947

5 Year Results of Treatment with Roentgen Rays, All Cases—Unclassified

Cases treated	139
Indeterminate cases	25
Cases followed	114
Number of 5 year cures	67
Determinate 5 year cure rate	59 per cent
Absolute 5 year cure rate	48 per cent

TABLE III

CANCER OF LARYNX AND LARYNGOPHARYNX, 1931–JUNE, 1947

Total Number of Cases Treated by Roentgen Irradiation	139
Indeterminate Cases	25

	Number of Cases	Over 70 Years of Age
Course of therapy not completed	5	4
Died of other causes, status of larynx *not* known	2	0
Died of other causes, with *no* evidence of disease in larynx	11	7
Lost to follow-up with no evidence of disease in larynx when last seen	7	2

The matter of indeterminate cases is a serious problem in the statistical evaluation of the results of treatment. There were 25 indeterminate cases in our series (Table III), 13 of which were patients over seventy years of age. There were 5 patients who did not complete therapy; 3 aged seventy-one, seventy-eight and eighty died of other causes during the course of treatment, while the other 2, aged sixty-nine and eighty, did not return. Death due to other causes occurred from a few months to nearly five years after therapy in 13 cases, in 11 of which there was no evidence of disease in the larynx at the time of death, while in the other 2 the status of the larynx was not known. There were 7 patients lost to follow-up from a few days to over two years after therapy who, when last seen, showed no evidence of disease in the larynx.

A better appreciation of the five year results of treatment may be obtained if the analysis is made on the basis of our method of classification. During the period of 1931 to June, 1947, 71 cases treated had intrinsic lesions, 56 of which were followed (Table IV). At the end of five years, there were 43 cases alive and free of disease. On

TABLE IV

CANCER OF INTRINSIC LARYNX: 5 YEAR RESULTS OF TREATMENT WITH ROENTGEN RAYS, 1931–JUNE, 1947

	Cases Treated	Cases Followed	5 Year Cures	Determinate 5 Year Cure Rate	Absolute 5 Year Cure Rate
All intrinsic lesions	71	56	43	77%	61%
Originally suitable for cordectomy	21	17	15	88%	71%
Originally would require laryngectomy	50	39	28	72%	56%

the basis of the determinate cases, this number represents a five year cure rate of 77 per cent, while, if the indeterminate cases are considered as failures, the absolute five year cure rate is 61 per cent. Of these 71 intrinsic cases, 21 were originally suitable for cordectomy by laryngofissure. The determinate five year cure rate for this highly favorable group was 88 per cent, while the absolute was 71 per cent. The remaining 50 patients with intrinsic lesions would have required laryngectomy had they been treated surgically. The determinate five year cure rate for this group was 72 per cent, the absolute rate 56 per cent. This is a particularly important group because the successfully treated patients did not have to have the larynx removed.

During this same period of observation, there were 68 extrinsic lesions, 58 of which were followed (Table v). The number of five year survivals, free of any evidence of disease, was 24. The determinate five year cure rate for all the extrinsic lesions was 41 per cent, the absolute 35 per cent. A more detailed analysis, however, reveals the significant influence of location of the tumor on the results of treatment. Of the 68 extrinsic lesions, 30 were located anteriorly in the epiglottis and false cord. The determinate five year cure rate for these anteriorly located lesions was 62 per cent, the absolute 60 per cent. In contrast, for the 23 lesions located posterolaterally in the aryepiglottic fold, arytenoid, pyriform sinus, or postcricoid region, the determinate five year cure rate was 23 per cent, the absolute 17 per cent. For the remaining 15 cases in which lesions were extensive, involving both anterior and posterolateral locations, the results of treatment were the least satisfactory, the determinate five year cure rate being only 17 per cent, the absolute 13 per cent.

FIXATION

The anatomical method of classification indicates only extent of disease. A factor of equal importance in prognosis is the degree of infiltration. For cancer of the larynx and laryngopharynx, the most important indication of the degree of infiltra-

TABLE V

CANCER OF EXTRINSIC LARYNX: 5 YEAR RESULTS OF TREATMENT WITH ROENTGEN RAYS, 1931–JUNE, 1947

	Cases Treated	Cases Followed	5 Year Cures	Determinate 5 Year Cure Rate	Absolute 5 Year Cure Rate
All extrinsic lesions	68	58	24	41%	35%
Anterior location	30	29	18	62%	60%
Posterolateral location	23	17	4	23%	17%
Extensive lesions (both anterior and posterolateral locations)	15	12	2	17%	13%

TABLE VI

CANCER OF LARYNX AND LARYNGOPHARYNX TREATED BY ROENTGEN RAYS, 1931–JUNE, 1947

Total Number of Cases Treated..... 139

EFFECT OF FIXATION OF LARYNGEAL STRUCTURES

	Cases Treated	Cases Followed	5 Year Cures	Determinate 5 Year Cure Rate	Absolute 5 Year Cure Rate
All cases					
With fixation.....	39	33	10	30%	26%
Without fixation.....	100	81	57	70%	57%
Intrinsic					
With fixation.....	9	7	3	43%	33%
Without fixation.....	62	49	40	82%	65%
Extrinsic					
With fixation.....	30	26	7	27%	23%
Without fixation.....	38	32	17	53%	45%

tion is fixation of one or both sides of the laryngeal structures. In the period 1931 to June, 1947, 39 of the total of 139 cases treated had fixation of the larynx, usually only on one side, occasionally both (Table VI). Of these 39 cases with fixation, 10 were alive and well at the end of five years, a determinate five year cure rate of 30 per cent and an absolute cure rate of 26 per cent, considerably lower than the cure rates for the entire series. There were 9 intrinsic cases with fixation contrasted with 30 extrinsic cases. The determinate five year cure rate for these intrinsic cases was 43 per cent, the absolute 33 per cent. For the similarly involved extrinsic cases, the determinate five year cure rate was 27 per cent and the absolute 23 per cent. In general, the patient's chance of cure by radiotherapy is reduced one-half if there is fixation. Thus, in all categories of classification, the presence of fixation of the laryngeal structures indicates a decidedly poorer but not hopeless prognosis.

TRACHEOTOMY

Another important factor in prognosis is tracheotomy, provided the tracheotomy is performed as an emergency measure for laryngeal obstruction, as was done in our series, and not as a prophylactic procedure. Tracheotomy was performed for laryngeal obstruction in 38 cases out of 139 treated during the period 1931 to June, 1947 (Table VII). In 22 of these 38 cases there was fixation of one or both sides of the laryngeal structures. At the end of five years, there were 8 cured cases, 5 of which were decannulated. The intrinsic cases requiring tracheotomy numbered 9, 3 of which survived five years, while the extrinsic cases numbered 29 with only 5 surviving five years.

TABLE VII

CANCER OF LARYNX AND LARYNGOPHARYNX, 1931–JUNE, 1947

Total Number of Cases Treated by Roentgen Rays..... 139

RESULTS IN CASES REQUIRING TRACHEOTOMY

	Tracheotomy Performed	5 Year Cures	Number of Cases Decannulated
Total.....	38*	8	5
Intrinsic.....	9	3	2
Extrinsic.....	29	5	3
Before therapy...	18	2	2
During therapy..	6	0	0
After therapy....	14	6	3

* 22 cases had fixation of one or both sides of larynx.

A significant factor is the time of the tracheotomy. It was performed before the onset of therapy in 18 cases; only 2 of these survived five years. In 6 cases it was performed during the course of therapy which was necessarily interrupted; none survived five years. In 14 cases, tracheotomy was performed after therapy, two to seven months in 11 of these cases; at longer intervals in the other 3 cases. In contrast to the previous groups, there were 6 survivals after five years in this postirradiation group. While the tumor itself is the usual cause of the laryngeal obstruction in those cases requiring tracheotomy before or during therapy, the cause of laryngeal obstruction after therapy may be irradiation edema and not necessarily recurrent or persistent neoplasm. Edema of the larynx, particularly of the arytenoids, is a frequent postirradiation finding, which may persist for several months and occasionally for years. A severe upper respiratory infection may seriously aggravate this edema and necessitate tracheotomy. Recent limited experience with cortisone seems to indicate that this edema may be decreased sufficiently to avoid the necessity of tracheotomy. Since edema may mask a recurrence, reduction of the edema by cortisone allows better examination of the larynx.

The prognosis in cancer of the larynx and laryngopharynx is therefore adversely affected when tracheotomy is required before or during the course of radiation therapy. Its necessity at that time is indicative of an extensive infiltrating tumor. The operative trauma, the mechanical irritation of the tube, and the radiation reaction in the stoma favor the complication of perichondritis and also add technical difficulties to the treatment. It is for these reasons that prophylactic tracheotomy is contraindicated.

LYMPH NODES

Palpable cervical lymph nodes were noted in 43 out of 139 cases treated in the period 1931 to June, 1947. Of these 43 cases, 10 were intrinsic and 33 were extrinsic lesions. There were 13 cases which survived five years, 2 intrinsic and 11 extrinsic. However, in this period, lymph node biopsy was not a routine procedure and therefore no statistical evaluation can be made of these observations. In 1 advanced intrinsic case which survived twelve years, palpable cervical lymph nodes appeared three years after the primary treatment and disappeared after another course of roentgen therapy. Unfortunately, there was no histopathological proof that these lymph nodes contained metastases. In 1 extrinsic case which has survived eighteen years, a palpable supraclavicular lymph node appeared five years after the initial course of roentgen therapy and this node disappeared after an intensive course of irradiation. In another extrinsic case which has survived fifteen years, enlarged cervical lymph nodes, originally present at the time of the primary roentgen treatment, were removed by a limited neck dissection and were proved histopathologically to be metastatic squamous cell carcinoma. This is the only cured case prior to 1947 for which there is histopathological proof of metastatic cervical lymph nodes. In the more recent cases, since 1947, aspiration biopsy is a routine procedure for all suspected cervical lymph nodes.

PROGNOSIS

From a prognostic point of view, a lesion may be classified as advanced if there is fixation, if there is laryngeal obstruction necessitating tracheotomy before or during radiation therapy, or if the lesion is located posterolaterally on the arytenoid, aryepiglottic fold, pyriform sinus, or postcricoid region. In our five year series (Table VIII), there were 61 such advanced lesions for which the determinate cure rate was 26 per cent and the absolute 21 per cent. The effect of cervical lymph node metastases was not evaluated because of lack of histopathological data. The surgical therapy for such advanced lesions would be extensive laryngectomy or laryngopharyngectomy, probably combined with radical

TABLE VIII

CANCER OF THE LARYNX AND LARYNGOPHARYNX TREATED BY ROENTGEN RAYS, 1931–JUNE, 1947

PROGNOSIS

	Cases Treated	Cases Followed	5 Year Cures	Determinate 5 Year Cure Rate	Absolute 5 Year Cure Rate
Limited lesions					
Intrinsic larynx, false cord and epiglottis					
Good mobility					
No obstruction	78	65	54	83%	69%
Advanced lesions					
Posterolateral location					
Laryngeal obstruction					
Fixation	61	49	13	26%	21%

neck dissection, but it is not yet known whether the results are any better with radical surgery than with radiation therapy. In marked contrast, however, are the results of roentgen therapy in the remaining 78 cases in which the tumor is limited to the intrinsic larynx, false cord, or epiglottis, with good mobility of the laryngeal structures and without laryngeal obstruction. The determinate five year cure rate for this group of cases is 83 per cent, the absolute 69 per cent. Included in this highly favorable group were our cases suitable for cordectomy, but 48 of the cases followed would have required laryngectomy had they been treated surgically originally. It is gratifying to report that 39 of these 48 cases, over 80 per cent, are not only alive and well but are in full possession of their larynxes with voice unimpaired. This group clearly indicates the good results that may be obtained if the selection of clinical material is made in favor of roentgen therapy.

TEN YEAR RESULTS OF TREATMENT

The ten year results of treatment (Table IX) were studied on the basis of 78 cases treated from 1931 to 1941. In general, the results at ten years are similar to those at five. The determinate ten year cure rate for the entire group was 52 per cent, the absolute 41 per cent. In this period there were 35 intrinsic lesions with 19 cures, for which the determinate ten year cure rate was 70 per cent and the absolute 54 per

TABLE IX

CANCER OF LARYNX AND LARYNGOPHARYNX TREATED BY ROENTGEN RAYS, 1931–1941

10 YEAR RESULTS OF TREATMENT

	Cases Treated	Cases Followed	10 Year Cures	Determinate 10 Year Cure Rate	Absolute 10 Year Cure Rate
All Cases	78	61	32	52%	41%
Intrinsic	35	27	19*	70%	54%
Extrinsic	43	34	13†	38%	30%

* 3 had fixed cords and 3 required tracheotomy, 1 before and 2 after therapy; 16 lesions would have needed laryngectomy.

† 3 had fixation, 1 had neck dissection for metastatic nodes, 1 required tracheotomy before therapy; 3 lesions involved arytenoid, pyriform sinus or postcricoid region.

cent. Had these surviving cases been treated surgically, 16 would have had the larynx removed, the other 3 having been suitable for cordectomy. Several advanced lesions were included in the cured cases, 3 with fixed cords and 3 which required tracheotomy, 1 before and 2 after therapy. The cases of extrinsic lesions numbered 43 with 13 cures, for which the determinate ten year cure rate was 38 per cent and the absolute 30 per cent. The 13 cured extrinsic cases included 10 lesions located anteriorly in the epiglottis and false cord, a location which has a relatively favorable prognosis. In 1 case, there was fixation of one side of the larynx and metastatic cervical lymph nodes which required neck dissection; in another case tracheotomy was required before therapy. The cured extrinsic cases also included 3 lesions in the posterolateral location, with involvement of the arytenoid, pyriform sinus or postcricoid region, and 2 of these were further complicated by fixation of one side of the larynx. The ten year results indicate that the prognosis for advanced cases is not hopeless and that some of them can be cured with preservation of the larynx.

POSTIRRADIATION SURGERY

A serious problem arises in the management of irradiation failures. The operations that have been performed for such cases are: total laryngectomy, hemilaryngectomy, laryngofissure, and transhyoid pharyngotomy for excision of the epiglottis. Despite opinions to the contrary, these operations have been done without unusual difficulty or complication. Postoperative healing and convalescence have been uneventful.

Total laryngectomy was performed for irradiation failures in 27 cases from 1931 to 1951 (Table x). In 23 cases, the operation was performed two to twelve months after radiation therapy, and in the other 4 at longer intervals. Only 2 of these laryngectomized patients have survived more than five years. Of the more recently operated cases, 3 are alive and well at two years, and 1 at one year. Of the two year survivals, 1 is a man aged seventy who had two intensive courses of radiation therapy without success before laryngectomy was done. Neck dissection was combined with laryngectomy in 3 cases without success. One laryngectomy followed an unsuccessful hemilaryngectomy performed one year previously, but this patient died postoperatively from a cerebral vascular complication.

TABLE X

CANCER OF LARYNX AND LARYNGOPHARYNX, 1931–1951

Total Number of Cases Treated by Roentgen Rays	220
POSTIRRADIATION SURGERY	
Total laryngectomies	27
Hemilaryngectomy	1
Cordectomy by laryngofissure	5
Excision of epiglottis	2
Neck dissection (combined with laryngectomy in 3)	8
Plastic repair	1

Cordectomy by laryngofissure was performed with apparent success in 5 cases of irradiation failure. In 1 case the larynx was free of disease when death from another cause occurred four years later. The other 4 cases were done within the past three years and are alive and well to date. The recurrences were detected two to ten months after irradiation in 4 cases and at fifteen months in the fifth case. In each case, the recurrent lesion was small and suitable for cordectomy. Of greater significance, however, is the fact that 3 of these cases were originally classified by the laryngologists as requiring laryngectomy had they not been treated by irradiation.

Excision of the epiglottis for recurrent disease was done within the past year in 2 cases, 1 of which is alive and apparently free of disease.

The management of metastatic lymph nodes presents the same problems in cancer of the larynx and laryngopharynx as it does with cancer originating elsewhere in

the head and neck. Neck dissections were performed in 8 cases. One patient is alive and well for fifteen years, 3 others for one to four years. While radical neck dissection for metastatic lymph nodes is possible without disturbing an intact previously irradiated larynx, 1 of these cases subsequently developed cartilage necrosis and required a tracheotomy, which is still present.

Plastic surgical repair of an area of radionecrosis of the neck by means of a tube pedicle graft was successfully accomplished in 1 case. In this case, a lesion which involved the epiglottis and false cord failed to respond to a course of roentgen therapy administered through a single anterior field. It was subsequently re-treated successfully by a second course of roentgen therapy directed through two opposing lateral fields. However, over a period of three years a 5 cm. circular area of skin over the hyoid bone broke down and separated out as a slough. After removal of the hyoid bone, plastic repair was performed with success.

Therefore, after properly administered radiation therapy to the neck for cancer of the larynx or laryngopharynx, major surgical procedures of curative value can be done.

SURVIVAL RATE

An over-all picture of the results of roentgen therapy in cancer of the larynx and laryngopharynx may be obtained by a study of the survival rate curves drawn for ten years. In Chart II these curves are shown for all cases and for the intrinsic and extrinsic lesions separately. In each category, the curve has been drawn for both the determinate and the absolute survival rates. The time of survival is reckoned from the first day of treatment to the date of death. In the case of persistent or recurrent disease successfully treated by surgery, the survival time following the successful surgery is not included in this chart.

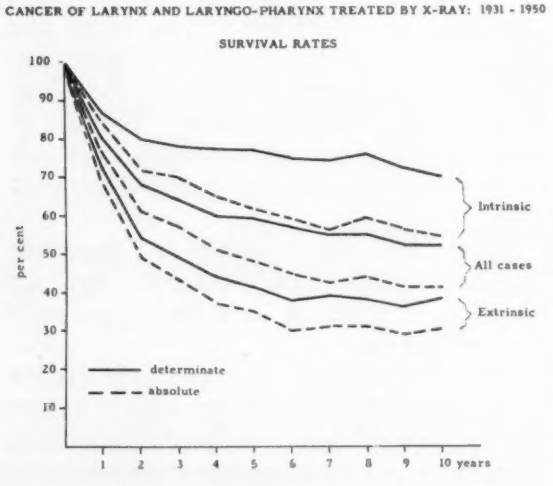

CHART II

These curves show that the survival rates fall rapidly in the first two years for both the intrinsic and extrinsic lesions. Thereafter there is a gradual levelling so that from the fifth year onwards, the survival rates remain fairly constant. From these curves we may deduce that most of the failures of radiation therapy should be apparent within one or two years. The probability of recurrence in cases that are well over two years gradually diminishes so that by five years a cured case may be expected to remain cured. Actually, in the 139 cases treated prior to June, 1947, only 2 cases developed recurrences after five years. Both were intrinsic lesions originally. One developed a postcricoid carcinoma in the twelfth year and the other developed a local recurrence on the vocal cord in the sixth year. Except for these 2 instances, we have had no recurrences after five years.

DISCUSSION

The value of roentgen therapy and the preference of irradiation to surgery have been controversial issues in the treatment of cancer of the larynx and laryngopharynx. Our experience of over twenty years with roentgen therapy in this disease was in the nature of a clinical investigation to help resolve this controversy.

With regard to the value of irradiation, our five and ten year results are practically equivalent to the surgical results for comparable material. Our clinical material was unselected since all cases, early stages as well as late, were treated.

Our results clearly demonstrate that the

earlier the stage of disease, the better the prognosis, as one may expect to find in the surgical management of laryngopharyngeal cancer. In the very advanced lesions which have extended into the posterolateral portion of the laryngopharynx or which have infiltrated the vocal cord or arytenoid to cause fixation, the survival rates are poor with any form of treatment; but some cures have been obtained with roentgen therapy and the prognosis is therefore not hopeless. At the other extreme are the highly favorable results obtained with roentgen therapy in small cordal cancers which were suitable for cordectomy, an operation for which there is also an equally high survival rate. Therefore, as far as survival is concerned, the results of radiotherapy and surgery in *comparable* material are almost identical.

Radiotherapy requires daily skilled attendance extending over a long period of time and may be followed by another long period of reaction with a varying degree of discomfort to the patient. There is also a small risk of serious complications such as obstructive edema, cartilage necrosis, or necrotizing pneumonitis, risks which are gradually being reduced by improvements in technique and by adequate supportive medical measures. Surgery, on the other hand, requires removal of the larynx in all cases except the early stages suitable for cordectomy or hemilaryngectomy. Notwithstanding the esophageal voice, loss of the larynx is a serious handicap to any patient. If the survival rate is the same, the method of choice is that one which would preserve the larynx intact as a functioning organ. It is for this reason that radiotherapy should be the method of choice for the majority of cases of cancer of the larynx and laryngopharynx. Laryngectomy is indicated for the irradiation failures, and with proper follow-up the failures can be detected at an early stage. No additional risks due to irradiation are incurred in the performance of the operation and cure is still possible in some cases.

An obvious exception to the rule that radiation therapy is the method of choice, with surgery reserved for irradiation failures, is the case with cartilage necrosis ab initio. It is well known that exposed infected cartilage cannot tolerate doses of radiation in the cancerocidal range and that the end result of treatment in such a case would be a radiation laryngectomy with its prolonged morbidity. Therefore, in the presence of exposed infected cartilage, laryngectomy would be the method of choice. An exception to this rule, however, is necrosis of the epiglottis which can heal after a course of radiation therapy.

It is often stated that fixation of the laryngeal structures is a contraindication to roentgen therapy. We usually interpret this finding as an indication of advanced infiltrating disease. It is also regarded by surgeons as an unfavorable prognostic sign. Although our results indicate that the survival rates are halved when fixation is present, an appreciable number of cures have been obtained with roentgen therapy. It is also frequently stated that subglottic extension of disease is a contraindication to roentgen therapy. While we did not make a separate classification of cases with subglottic extension in this paper, we found that the prognosis of each case was dependent upon other findings in the laryngeal status rather than subglottic extension.

Therefore, with the exceptions as discussed, we believe that radiation therapy at the present time is the method of choice in the treatment of cancer of the larynx and laryngopharynx. It is our opinion that the best interests of the patient are served by this policy.

SUMMARY

1. From 1931 to 1951, 220 cases of cancer of the larynx and laryngopharynx have been treated by roentgen irradiation as the method of choice.

2. These cases have been classified into two major anatomical groups, the larynx proper, or intrinsic larynx, and the laryngopharynx, or extrinsic larynx, with significant subgroups.

3. The age group fifty to sixty-nine accounts for three-fifths of all the cases; 20 per cent of the cases occur after the age of

seventy years. The male to female ratio is 9 to 1.

4. A histopathological report of squamous cell carcinoma was obtained in all cases except 2 in which it was adenocarcinoma.

5. Until 1947, all cases were treated with 200 kv. radiation through two directly opposing lateral neck fields for a mid-laryngeal tumor dose of 4,700 to 6,000 roentgens in twenty-eight to forty days. Since 1947, the technical change has been in the direction of higher kilovoltage radiation, greater tumor dose and longer protraction.

6. Five year results were based upon 139 cases treated from 1931 to June, 1947. The determinate five year cure rates were 59 per cent for all cases, 77 per cent for the intrinsic group, and 41 per cent for the extrinsic. The intrinsic and extrinsic subgroups show significant differences. Absolute cure rates are appreciably lower because of the large number of indeterminate cases.

7. Analysis of the indeterminate cases reveals more than half of these patients to be over seventy years of age.

8. The significance of infiltration, as indicated by fixation of one or both sides of the larynx, is revealed in lower survival rates when fixation is observed.

9. The significance of laryngeal obstruction, as indicated by the necessity of tracheotomy before or during therapy, is revealed in the very poor prognosis of these cases.

10. No statistical deductions are made with regard to cervical lymph node metastases because of the lack of histopathological proof.

11. The ten year results of treatment are essentially similar to those at five year and include an appreciable number of advanced cases.

12. Study of the survival rate chart reveals that most of the recurrences take place within the first two years and a few may occcur up to the fifth year but that after five years recurrences are very rare.

13. Radiation therapy is contraindicated in the presence of cartilage necrosis because the larynx cannot be preserved and the radiation morbidity is prolonged. An exception to this rule is necrosis of the epiglottis.

14. Statements regarding fixation and subglottic extension of disease as contraindications to radiation therapy are discussed.

15. Surgical procedures of a limited, advanced, or radical nature are possible in the case of failure after a properly administered course of radiation therapy, with successful outcome in a small number of patients.

16. Radiation therapy and cordectomy are considered equal choices for the early cordal lesions.

17. Since the value of radiation therapy is practically the same as that of surgery, as far as survival is concerned, radiation therapy should be the method of choice over surgery where it is a matter of preservation of the larynx.

18. In limited lesions without fixation and without obstruction, high cure rates may be obtained.

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REFERENCES

1. BACLESSE, F. Roentgentherapy of carcinoma of larynx. *J. Fac. Radiologists*, 1951, *3*, 3–12.
2. BLADY, J. V., and CHAMBERLAIN, W. E. Treatment of cancer of larynx by roentgen irradiation. AM. J. ROENTGENOL. & RAD. THERAPY, 1944, *51*, 481–495.
3. CUTLER, M. Cancer of larynx; five-year results of radiotherapy. *Radiology*, 1948, *51*, 509–520.
4. FALBE-HANSEN, J. Surgical treatment of cancer laryngis, with special reference to results of laryngectomy. *Acta oto-laryng.*, 1951, Supp. 95, pp. 212–236.
5. GOODRICH, W. A., and LENZ, M. Laryngeal chondronecrosis following roentgen therapy. AM. J. ROENTGENOL. & RAD. THERAPY, 1948, *60*, 22–28.
6. HARRIS, W. Roentgentherapy for cancer of larynx. *J. Fac. Radiologists*, 1951, *3*, 35–39.
7. HARRIS, W., and KLEMPERER, P. Pathologic differentiation between radiosensitive and

nonradiosensitive malignant neoplasms of larynx. *Arch. Otolaryng.*, 1938, *28*, 355–363.

8. Harris,, W., Kramer, R., and Silverstone, S. M. Roentgen therapy for carcinoma of larynx. *Radiology*, 1948, *51* 708–718.
9. Harris, W., Kramer, R., and Silverstone, S. M. Radiation Therapy for Cancer of the Larynx. In: Clinical Therapeutic Radiology. U. V. Portmann, Editor, Thomas Nelson & Sons, New York, 1950.
10. Leborge, F. E. Roentgentherapy of cancer of larynx. *J. Fac. Radiologists*, 1951, *3*, 24–28.
11. Lederman, M. Classification of laryngeal cancer from radiotherapeutic viewpoint. *Brit. J. Radiol.*, 1943, *16*, 298–300.
12. Nielson, J., and Strandberg, O. Roentgen treatment in cancer of larynx. *Acta radiol.*, 1942, *23*, 189–208.
13. Som, M. L. Limited surgery after failure of radiotherapy in treatment of carcinoma of larynx. *Ann. Otol., Rhin. & Laryng.*, 1951, *60*, 695–703.

ROENTGEN THERAPY OF HEPATIC METASTASES*

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METASTATIC cancer is found in the liver in about one-third of the cases of malignant disease coming to autopsy, and hepatic failure is often the immediate cause of death. Sometimes there may be few or no symptoms, but in many patients the last few months of life are heavy with suffering from pain, prostration, abdominal distention and fever. Medical treatment seldom affords much relief of such symptoms.

The common cancers such as those of the breast, lung, stomach, colon and rectum are also those which have a high incidence of liver metastases[1,2,9,14] (Table 1)—25 to 50 per cent—so that the increasingly successful control of the primary tumors by modern methods of treatment is only too often frustrated by the early development of liver metastases. Pulmonary metastases are beginning to yield to the combined efforts of chemotherapist and radiotherapist. Brain metastases have for years afforded one of the more striking successes of radiotherapy, but liver metastases have always been regarded as a hopeless proposition, mainly from fear of irreversibly damaging the surviving liver parenchyma.

TABLE I

INCIDENCE OF LIVER METASTASES IN VARIOUS TYPES OF CANCER

Primary Site	Liver Metastases Per Cent at Autopsy
Cancer of the breast	50
Cancer of the bronchus	40
Cancer of the stomach	40
Cancer of the colon and rectum	45
Cancer of the esophagus	25

Although successful irradiation of the liver in cases of neuroblastoma,[12,16] and malignant lymphoma is by now well documented, and although Case and Warthin[4] as long ago as 1924 reported that the cells of the liver were much less radiosensitive than the epithelium of the smaller bile ducts or the mucous membrane of the gastrointestinal tract, the general impression has persisted among radiologists that it is dangerous to irradiate the liver. Pack and Livingston,[11] for example, state that the liver parenchyma is as radiosensitive as the metastatic carcinoma, and only Cade[3] among the writers of major textbooks insists that the dangers of irradiating the liver have been exaggerated. One of the supposed dangers of irradiation is the initial swelling of the cancer cells, which, together with intercellular edema, might further compress the liver parenchyma and precipitate the onset of hepatic insufficiency. For this reason when one of us first treated liver metastases in 1941, the tumor dose of 2,000 roentgens at 1,000 kilovolts was spread out over a period of four weeks; no parenchymal damage was observed, and although some symptomatic relief was obtained, it was felt that the month in the hospital was too large a fraction of the remaining life expectancy to be worth while to the patient.

Karnofsky and his associates[8] showed, that with nitrogen mustard tumor regression occurred without an initial period of edema and they therefore suggested that if roentgen therapy was immediately preceded by a single intravenous dose of nitrogen mustard—0.4 mg. per kilogram body weight—the initial radiation edema would be prevented, and an adequate tumor dose could be given in a few days instead of weeks. At first a tissue dose of

* Presented at the Thirty-fifth Annual Meeting, American Radium Society, St. Louis, Mo., April 20–22, 1953.

TABLE II

SUMMARY OF PRESENT SERIES

Primary Site	No. of Cases	Per Cent Improved		Average Duration of Improvement in Months	Cause of Death		Others
		Symptoms	Lab. Tests		Liver Metastases	Radiation Damage	
Breast	9	66	66	1.6	4	1(?)	4
Bronchus	5	100	60	2.7	3		4
Gastrointestinal tract	20	70	75	1.2*	11	2	5
Others	2	50	50	1.5	1		1

* 6 unknown.

2,000 r was given to the whole liver in eight days at 1,000 kv.; the dose was increased by increments of 500 r to 3,500 r, and finally in 6 cases 3,750 r was given. Relief of symptoms was obtained in 26 out of 36 cases treated, liver function as judged by laboratory data was improved in 17 cases, and evidence suggestive of liver damage was found in only one questionable instance (Table II). The duration of the improvement was short, and symptoms recurred on the average in rather less than two months; however, in 14 cases the liver metastases were not the immediate cause of death.

In this series the whole liver has been irradiated through opposed anterior and posterior fields at 1,000 kv., half-value layer 3.8 mm. Pb; with this quality radiation, the tissue dose throughout the irradiated volume is approximately the same as the skin dose on each field (Fig. 1). The area of each field was seldom less than 400 sq. cm., so that the integral dose was high, ranging from 25 to over 100 megagram-r

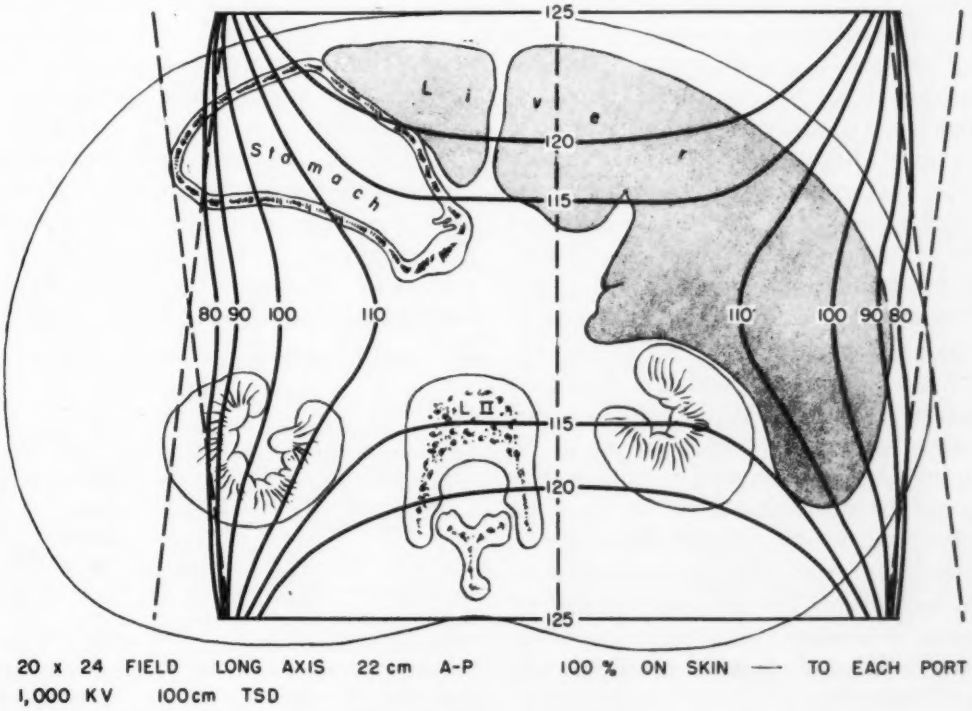

FIG. 1. Isodose distribution.

TABLE III

IRRADIATION TECHNIQUE: OVER-ALL TIME 8 DAYS

Average Field Size	Average Anteroposterior Diameter	Skin Dose	Tumor Dose	Integral Dose
cm.	cm.	r	r	megagram-r
18×24	20	1,820	2,000	27
22×22	23	3,230	3,000	56
23×26	22	3,570	3,500 and 3,750	74

Factors: 1,000 kv., half-value layer 3.8 mm. Pb, 45 r/min. at 100 cm. focus skin distance
90 r/min. at 70 cm. focus skin distance
Nitrogen mustard: 0.4 mg. per kilogram body weight, intravenously

$$\text{Integral dose} = k \times \text{surface dose in r} \times \frac{100 - \text{per cent exit dose}}{100}$$

$$k = 1.44 \times \text{field area} \times \text{depth of 50 per cent depth dose} \times \frac{1 + 2.88 d^{\frac{1}{2}}}{FDS}$$

(Table III). There was, however, no evidence of systemic radiation intoxication even with the highest integral dose, nor did irradiation of the liver aggravate the temporary bone marrow depression produced by nitrogen mustard.

The dominant symptoms of hepatic metastases are prostration, anorexia and pain; satisfactory relief of weakness and fatigue was obtained in 17 out of 31 cases, of anorexia in 20 of 31 cases, and of pain in 26 of 30 cases. The relief of pain in so many instances is especially gratifying; being due to stretching of the hepatic ligaments and capsule, it is obstinately resistant to all forms of medication, and there is the further difficulty that in the presence of liver damage opiates and sedatives are poorly tolerated and perhaps tend to precipitate the onset of hepatic coma.[13] Abdominal distention was relieved in 12 out of 17 cases, nausea and vomiting in 7 of 16, and sweating and fever in 11 of 18 cases. Profuse sweating, especially at night, is one of the most trying symptoms of hepatic metastases, and its cessation during treatment is a useful sign that improvement in the patient's general condition will follow (Table IV).

Extensive liver function studies have been carried out in most of the patients and will be fully reported elsewhere.[6] The individual data are summarized in Table V; there was improvement or no impairment in 23 out of 31 cases, while 8 cases showed continued deterioration.

The material is insufficient for the determination of the optimum tumor dose. From Table VI it can be seen that about the same proportion of symptomatic relief and improved liver function was obtained at each dose level from 2,000 r to 3,750 r. However, tissue doses of 3,500 r and upwards entail an increasing risk of mucosal ulcerations in the gastrointestinal tract, particularly in the transverse colon. Four patients had persistent diarrhea following treatment, which was assumed to be due to intestinal damage. Two of the patients who received

TABLE IV

SUMMARY OF EFFECTS ON SYMPTOMS

Symptoms	No. with Symptoms	No. Completely Relieved	No. Unchanged
Hepatic pain	30	26	4
Abdominal distention	17	12	5
Sweating and fever	18	11	7
Anorexia	31	20	11
Weakness and fatigue	31	17	14
Nausea and vomiting	16	7	9

Table V

SUMMARY OF EFFECTS ON LIVER FUNCTION

Test	Before Treatment		Within 3 Weeks After Treatment		
	Normal	Impaired	Improved	No change	Impaired
Bromsulphalein	0	30	17	7	6
Bilirubin	18	13	9	19	3
Alkaline phosphatase	2	28	16	9	5
Albumin	21	7	1	24	3
Globulin	21	7	1	24	3
Thymol	15	15	8	18	4
Cephalin-cholesterol flocculation	14	15	6	20	3
Cholesterol: Total	11	17	11	17	0
Free	10	18	11	17	0
Esters	10	18	10	18	0
Per cent free	16	12	6	21	1
Prothrombin	14	15	8	19	2

a tumor dose of 3,750 r in eight days experienced severe abdominal pain with signs of ileus a few days later; they died five weeks and seven weeks respectively from the end of the roentgen treatment. In both cases the primary cancer was an adenocarcinoma of the rectosigmoid; at autopsy both showed extensive ulcerative colitis, which was attributable to radiation damage; in neither case was there any evidence of radiation damage to the liver parenchyma. One of them had multiple hepatic metastases which showed varying degrees of necrosis and replacement fibrosis; the other had a single hepatic metastasis which measured 11 cm. in diameter at autopsy and was completely necrotic and surrounded by a fibrous capsule.

Possible renal damage was encountered in 2 instances; in one the tissue dose was only 1,800 r, and, although the patient had an elevated blood urea nitrogen before his death from cardiac failure, it seems unlikely that irradiation was the cause of the renal failure. In the second case the tumor dose was 3,750 r and the elevated blood urea nitrogen was probably due to radiation damage to the kidneys, but the damage was transitory, since normal renal function was restored some time before her death from disseminated cancer.

With one possible exception, none of the cases had radiation damage to the liver parenchyma. The exception was a patient with a carcinoma of the stomach and an enlarged liver which was presumed to be due to metastases; a positive aspiration biopsy was not obtained, but the liver was irradiated to a tissue dose of 3,500 r; the patient died five months after treatment,

Table VI

CORRELATION OF RESULTS WITH TUMOR DOSE

Tumor Dose r	No. of Cases	No. Improved		No. Unchanged	No. with Radiation Damage		
		Symptoms	Lab. Tests		Liver	Kidney	Gastrointestinal Tract
2,000	5	3	—	2	0	1(?)	0
3,000	14	10	9	4	0	0	0
3,500	11	9	8	2	1(?)		2(?)
3,750	6	4	5	2	0	1	4

and autopsy revealed cirrhosis of the liver without metastases or evidence that there had been metastases which had been destroyed by the irradiation.

The type of cancer would be expected to influence the results of treatment, and we have the clinical impression that patients with hepatic metastases from cancer of the breast and from cancer of the lung respond better than those with cancer of the gastrointestinal tract. However, the material is insufficient for statistical conclusions, as 14 out of 20 cases with a gastrointestinal primary cancer obtained relief of symptoms, 6 out of 9 cases with a mammary primary, and all 5 cases with a bronchial cancer (Table VII). Nevertheless, our tentative conclusion on the optimum tumor dose for satisfactory palliation favors 2,500–3,000 r for hepatic metastases of mammary or bronchogenic carcinoma, but 3,000–3,500 r for those of gastrointestinal origin.

TABLE VII

CORRELATION OF RESULTS WITH TYPE OF CANCER

Primary	No. of Cases	No. Improved		No. Unchanged
		Symptoms	Lab. Tests	
Breast	9	6	6	3
Bronchus	5	5	3	0
Gastrointestinal tract	20	14	12	6
Others	2	1	1	1

In any clinical investigation it is inevitable that the planned treatment has to be modified according to the condition of individual patients. The planned treatment in an over-all time of eight days was carried out in 24 of the 36 cases, but in 6 the time was extended to fifteen days, and in another 6 to twenty-two days. The results in the three groups (Table VIII) do not show any significant difference, but from the patient's point of view the shortest time of treatment means less expense and a longer time at home to gather such benefits as treatment has afforded.

A second modification in the plan was made early in the investigation when it was suggested that the effects of roentgen therapy alone without preliminary nitrogen mustard should be evaluated. It was recalled that the radiotherapists of thirty years ago, when massive single dose treatments were the rule, were not apparently afraid of radiation edema. Our results show that they were justified, for there were no disastrous effects on liver function in the 22 cases of this series treated by roentgen rays alone. It seems possible that the magnitude of the initial dose—500 r to 800 r—causes such rapid shrinkage of the metastases that there is plenty of room within the liver capsule for whatever edema may also be produced. There was no significant difference in the results of roentgen therapy alone compared with combined nitrogen mustard and roentgen therapy; 16 of 22 cases in the former group obtained symptomatic relief, and 10 of 14 in the latter group; liver function tests showed improvement in 16 of the roentgen therapy group and in 6 of the combined therapy group (Table IX). However, the tumor dose was

TABLE VIII

INFLUENCE OF OVER-ALL TIME OF ROENTGEN TREATMENT

Over-all Time Days	No. of Cases	No. Improved		No. Unchanged
		Symptoms	Lab. Tests	
8	24	17	16	7
15	6	4	2	2
22	6	5	4	1

TABLE IX

COMPARISON OF COMBINED CHEMOTHERAPY AND ROENTGEN THERAPY WITH ROENTGEN THERAPY ALONE

Treatment	No. of Cases	No. Improved		No. Unchanged
		Symptoms	Lab. Tests	
Combined treatment	14	10	6	4*
Roentgen therapy only	22	16	16	6

* 2 unknown.

TABLE X

INCIDENCE OF VOMITING DUE TO TREATMENT

Treatment	No. of Cases	No. of Patients Vomiting			No Vomiting at any Time
		1st day only	3 days only	7 days or more	
Combined treatment	14	10	1	1	2
Roentgen therapy only	22	9	6	3	4

somewhat lower in the combined therapy group than in the roentgen therapy group, so that more cases are required before a valid assessment can be made.

Nitrogen mustard often causes vomiting during the first twelve hours after administration, and it would be expected that these massive doses of roentgen radiation would also cause severe vomiting. With combined therapy only 2 of 14 patients had no vomiting at all, and with roentgen therapy alone 4 of 22 patients; however, in the combined therapy group only 2 patients vomited after the first day, whereas in the roentgen therapy group 9 had persistent vomiting (Table x). It seems possible, therefore, that the combination of nitrogen mustard with roentgen therapy causes less vomiting than roentgen therapy alone.

The longest survival of any patient in this series was seven months, and the data in his case form a convenient summary of the results of this investigation (Fig. 2).

The patient was sixty-one years old and was admitted on February 2, 1952, complaining of severe pain in the right upper quadrant of the abdomen, complete loss of appetite and such a degree of prostration that he could not get out of bed. The whole liver was grossly enlarged, the lower border of the right lobe being 2 cm. below the level of the umbilicus; aspiration biopsy of the liver confirmed the clinical diagnosis of hepatic metastases secondary to an anaplastic epidermoid carcinoma of the

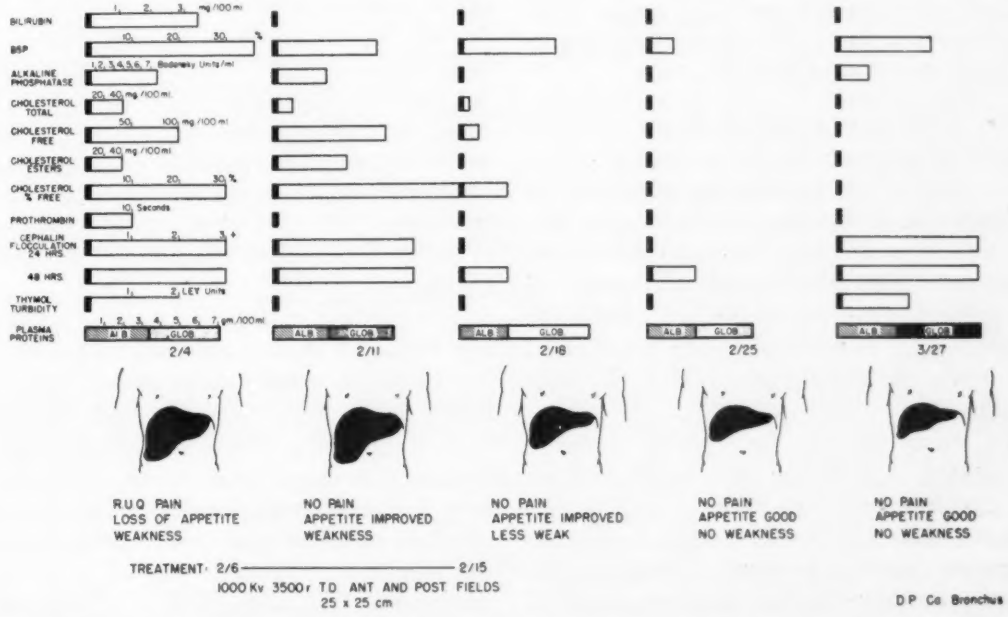

FIG. 2. To show the improvement in symptoms and liver function tests. The black rectangle represents in each case the normal values and the figures over the white rectangle must be added to the normal value to give the actual values measured.

bronchus. From February 6 to 15 a minimum tumor dose of 3,500 r was delivered to the whole liver through 25 by 25 cm. anterior and posterior fields at 1,000 kv.; the integral dose was 72 megagram-r. By February 11 his pain had completely disappeared and his appetite was better; a few days later he was able to walk about and by Feburary 25 he felt entirely well. The serum bilirubin was 5.0 mg. on February 4, and normal (0.2 mg.) on February 11. The bromsulphalein retention was 41 per cent on February 4 and fell steadily to 10 per cent on February 25. The serum alkaline phosphatase was 12.5 Bodansky units on February 4, and had fallen to normal by February 18. The elevated serum cholesterols had all become normal by February 25, and the prothrombin time of 24 seconds before treatment became normal (16 sec.) on February 11; the 3 plus cephalin flocculation test before treatment was negative on February 18. The only test which did not show any improvement was the reversed albumin-globulin ratio. The liver, ten days after treatment, had diminished to half its pretreatment size; seven weeks after treatment the patient was still entirely well, but the liver was slightly larger and the liver function tests were again becoming abnormal. The patient remained entirely well for seven months after treatment and then developed recurrent cancer in the remaining left lung and in the liver. For the last two weeks of life he had severe anorexia and increasing ascites and died on September 30, 1952; there was no autopsy.

The work here reported deals with the relief of agonies of the flesh; agonies of the spirit are no less important, especially in patients who know the nature of their disease and its prognosis. The feeling that they have not been abandoned and that all the present resources of medical care have been afforded them has been a great comfort both to the patients and to their families.

We have not so far treated hepatic metastases in patients who have had no symptoms referable to them, and although we have shown that it is possible to obtain regression and apparently complete destruction of established metastases without damage to the vital functions of the liver or other tissues within the irradiated volume, it cannot be assumed that late changes such as cirrhosis of the liver might not occur. With this proviso, it might be justifiable to offer treatment to less advanced cases even if asymptomatic, especially if the liver metastases could be positively diagnosed while still small. Furthermore, there are other therapeutic combinations as yet untried, such as hormone therapy,[5,7] virus therapy[13] or ligation of the hepatic artery.[10] The justification for the existence of special cancer centers is the spirit of hope which pervades them and their willingness to attempt the hitherto impossible. To the Director of Memorial Cancer Center and to our colleagues we are deeply grateful for their enthusiasm and support which alone made this investigation possible.

SUMMARY

The results of treatment of hepatic metastases secondary to carcinoma of the breast, bronchus and gastrointestinal tract, are reported in 36 patients; symptomatic improvement was obtained in 26 patients.

The symptomatic relief of pain, anorexia, nausea, vomiting, weakness, fatigue, sweating and abdominal distention was accompanied by reduction in the size of the enlarged liver, by gain in body weight, and by improvement in liver function as measured by determination of the serum bilirubin, alkaline phosphatase, cholesterols and proteins, and by the bromsulphalein retention test, the prothrombin time, the cephalin flocculation test and the thymol turbidity.

The method of treatment was supervoltage roentgen therapy alone in 22 cases; in 14 cases a single intravenous dose of nitrogen mustard (0.4 mg. per kilogram body weight) was given immediately before the first roentgen treatment. The whole liver, however large, was irradiated through opposed anterior and posterior fields, and the tumor dose ranged from 2,000 to 3,750 roentgens. The over-all time of treatment was eight days in 24 cases, fifteen days in 6 cases, and twenty-two days in 6 cases.

No evidence of liver damage was observed at any dose level. The dose levels of 3,500 r and 3,750 r, however, carry an increasing risk of damage to the mucous membrane of the gastrointestinal tract, and particularly to the transverse colon.

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REFERENCES

1. Abrams, H. L., Spiro, R., and Goldstein, N. Metastases in carcinoma; analysis of 1000 autopsied cases. *Cancer*, 1950, *3*, 74–85.
2. Ackerman, L. V., and del Regato, J. A. Cancer: Diagnosis, Treatment and Prognosis. C. V. Mosby Company, St. Louis, 1947, p. 668.
3. Cade, S. Malignant Disease and Its Treatment by Radium. Second edition. John Wright & Sons, Ltd., Bristol, 1948, Vol. I, p. 208.
4. Case, J. T., and Warthin, A. S. Occurrence of hepatic lesions in patients treated by intensive deep roentgen irradiation. Am. J. Roentgenol. & Rad. Therapy, 1924, *12*, 27–46.
5. Escher, G. C. Hormone therapy in advanced mammary carcinoma. *Med. Clin. N. America*, 1952, *36*, 681–688.
6. Hamilton, L. D. Effects of irradiation and nitrogen mustard on liver function. To be published.
7. Hayes, M. A., Hodgson, P. E., and Coller, F. A. Use of testosterone in preventing postoperative liver dysfunction in the poor risk surgical patient. *Ann. Surg.*, 1952, *136*, 643–658.
8. Karnofsky, D. A., Abelmann, W. H., Craver, L. F., and Burchenal, J. H. Use of nitrogen mustards in palliative treatment of carcinoma; with particular reference to bronchogenic carcinoma. *Cancer*, 1948, *1*, 634–656.
9. Liljencrantz, E. Editor. Cancer Handbook of the Tumor Clinic. Stanford University School of Medicine, Stanford Univ. Press, Stanford University, Calif., 1939, p. 10.
10. McFadzean, A. J. S., and Cook, J. Ligation of splenic and hepatic arteries in portal hypertension. *Lancet*, 1953, *1*, 615–622.
11. Pack, G. T., and Livingston, E. M. Editors. Treatment of Cancer and Allied Diseases. Paul B. Hoeber, Inc., New York, 1940, p. 1092.
12. Phillips, R. Neuroblastoma. *Ann. Roy. Coll. Surgeons England*, 1953, *12*, 29–48.
13. Southam, C. M., and Moore, Alice E. Clinical studies of viruses as antineoplastic agents, with particular reference to Egypt 101 virus. *Cancer*, 1952, *5*, 1025–1034.
14. Willis, R. A. The Spread of Tumors in the Human Body. Second edition. Butterworth & Company, London, 1952, p. 180.
15. Wise, R. A. Etiology and treatment of hepatic coma. *South .Med. J.*, 1952, *45*, 716–722.
16. Wittenborg, M. H. Roentgen therapy in neuroblastoma. Review of 73 cases. *Radiology*, 1950, *54*, 679–687.

DISCUSSION

Dr. Irving M. Ariel, New York, N. Y. It is truly a pleasure and an honor to discuss Dr. Phillips' paper. It is a pleasure because all his writings and data are so nicely conceived and so brilliantly presented that they speak for themselves; it is an honor because I consider this subject of great fundamental importance.

As a result of past concepts of the danger of irradiation of the liver, an entire sector of the population afflicted with cancer has been deprived of the benefit of irradiation to the liver. It becomes increasingly important now to help these patients and to give them treatment. And, because of the advent of radioactive isotopes, the liver will be irradiated more and more, and it is essential to understand how the liver reacts to irradiation.

I think Dr. Phillips' data have once and for all dispelled the fear and pessimism which has encroached upon all thought pertaining to irradiation of the liver. Patients with liver cancer can be irradiated.

His use of the million volt unit is not permitted to many of us since we do not have that equipment. We have been irradiating patients usually with the conventional 250 kv. unit, with similar results. They tolerate it well. We have given 300 r through a 20 by 20 cm. port in a day. We are not afraid of the edema, Dr. Phillips. We think that is another factor which is exaggerated in the dangers of radiation intoxication and which is not too important.

My interest in this subject started when I wrote a paper for admission to this Society on the effects of a massive dose of irradiation to the rabbit liver. We gave doses of from 500 to 100,000 r to intensify the reactions so we could study them. We found that edema was not more marked in the liver than in other locations, and the edema was both extra- and intracellular edema.

I think the use of nitrogen mustard and the roentgen ray is excellent for this type of cancer, but I do not think the use of nitrogen mustard before giving the roentgen treatment is necessary to prevent radiation sickness. We

used the nitrogen mustard in our patients, and they are showing good results, at least temporarily.

One patient treated by Dr. Pack in 1942 for hemangioma (proved at operation) received a total of 3,000 r in twenty-one days, and he is now well.

We have had some rather interesting experiences with patients who were extremely ill. Those in a state of almost hepatic coma can be benefited temporarily by the use of cortisone, which exerts a beautiful temporary effect, and has permitted the use of irradiation to patients severely ill from cancer.

There are two questions I would like to ask of Dr. Phillips. First, does he have any ideas about the use of grid therapy with conventional x-ray units, irradiating the liver? Secondly, although we are sympathetic with the idea of administering the radiation as quickly as possible—as he has done in these patients—and administering it in eight days, how much is lost from the standpoint of the over-all protraction and fractionation as in the usual philosophy of administering radiation therapy?

From the standpoint of total dosage, we have got up to 4,000 r total dose in twenty-one days, and it has been nicely tolerated. I became overambitious with one patient who tolerated it very well, showing a nice symptomatic improvement, and gave him a total dose of 5,000 r in twenty-eight days, and he began to suffer marked anorexia, with impairment of liver function. I think the final total dosage still has to be worked out.

DR. CHARLES L. MARTIN, Dallas, Texas. I would like to ask Dr. Phillips if he made a study of the microscopic changes, if any, found at autopsy in the metastastic nodules in the livers of the patients treated with his technique.

DR. PHILLIPS (closing). In reply to Dr. Martin, the autopsy findings in 12 cases showed varying degrees of necrosis of the metastases in the liver in 10 cases, but in 2 cases there were no visible radiation effects. Our pathologist has noted an extreme fibrous encapsulation of the metastases, which is not the usual finding in nonirradiated cases. In only 1 case was there complete disappearance of all cancer cells; this was the case with a solitary metastasis measuring 11 cm. in diameter at autopsy; it was completely necrotic, surrounded by a thick fibrous capsule.

I am very grateful to Dr. Ariel for his generous remarks and interesting suggestions. I did not mention the use of 250 kv. roentgen rays because we have no personal experience of their value in palliating hepatic metastases; 1,000 kv. makes the treatment easier, I think, owing to the better dose distribution, less skin reaction and smaller integral dose.

The main reason for making the over-all treatment time as short as possible is that, being purely palliative, it is not too costly to the patient in either time or money.

Grid therapy is perhaps rightly called the poor man's supervoltage; we have not used it for hepatic metastases, but I think it should work satisfactorily.

VOL. 71, NO. 5

PHYSICAL MEASUREMENTS OF RADIATION THROUGH A GRID

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THIS paper presents the results of measurements, made in a phantom, of the intensity and distribution of roentgen rays from a 200 kv. (peak) generator after passing through a lead rubber grid.

FIG. 1. Roentgenogram showing streamers of radiation passing through a grid.

The claimed therapeutic advantage of a grid is not original with the authors[2] but a discussion will be included for completeness. Marks,[6] using a square hole lead rubber grid, gave patients radiation of such a value that desquamation and denudation of skin occurred. However, the radiation entered through separated multiple ports, so that there was tissue under the lead which received much less radiation. As a result, there were islands of "under-irradiated" skin which formed foci for rejuvenation, when the grids were placed so that the same areas were always protected in successive treatments.

At the tumor level, the incident beams have been scattered, so that a fairly uniform dosage distribution results at a given depth. Figure 1 is a roentgenogram of the streamers of radiation passing vertically through a grid. Two phenomena are apparent: (1) the divergence of the streamers, and (2) the decrease in contrast at the lower depths due to penumbra effects and scattering. If there is enough scattering, a level isodose curve should result.

Since there are foci of healthy tissue to promote healing, a higher skin dose is permissible with this technique. A numerical example is presented to illustrate the reported advantages of a grid. If 3,000 roentgens (in air) are delivered to a 20 by 20 cm. port (200 kv., peak, 1 mm. Cu half-value layer), the depth dose is 61 per cent, or 1,830 r at 10 cm.[1] Using the grid, the depth dose at 10 cm. is in the order of 25 per cent (using the same factors). An air dose of more than 10,000 r has been given,[6] resulting (for 25 per cent depth dose) in a tumor dose of more than 2,500 r.

It was felt by the authors that a grid made with round holes would be an improvement over the square hole type used by Marks, since the circumference would be smaller for a given exposed area, and this might lead to better healing. The Medical Department concurred and this investiga-

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tion was undertaken. Clinical applications are being made at this institution in the treatment of bronchogenic carcinoma and carcinoma of the cervix uteri. The results of this work will be presented in a later paper by Dr. B. P. Widmann of this department.

In designing useful grids, a problem to be solved was the arrangement of the holes. The holes could be cut with centers at the corners of a square lattice, or at the corners of an equilateral triangle lattice. The object was to get the maximum distance between hole edges for a particular hole diameter and per cent exposed area. It can be shown that the triangular lattice fulfills this requirement. Table 1 is a comparison of the two lattices for the particular case where the exposed area equals the unexposed area.

TABLE I

COMPARISON OF TRIANGULAR AND SQUARE LATTICE HOLE ARRANGEMENT

(50% of Skin Beneath Grid Exposed)

Hole Diameter	Triangular Lattice		Square Lattice	
	Center separation	Edge separation	Center separation	Edge separation
cm.	cm.	cm.	cm.	cm.
1.0	1.348	0.348	1.253	0.253
1.5	2.022	0.522	1.879	0.379
2.0	2.696	0.696	2.506	0.506

It is seen from Table 1 that the triangular lattice permits a greater distance between holes, and it was felt that this would promote healing.

The method of making grids used in this investigation is of interest. Hole centers were located 2 cm. apart, using a scale and 30°–60° triangle, for convenience of layout. The grids were made of 1 mm. equivalent lead rubber. They were cut using a 1.43 cm. diameter standard brass cork cutter. The resulting grid exposes 46 per cent of the skin beneath it.

Preliminary measurements were made to find the optimum hole diameter. A masonite phantom and a 25 r Victoreen chamber were used. The phantom construction was checked by taking readings at various depths without the grid, and the values obtained agreed with the published data to within 2 per cent.[1]

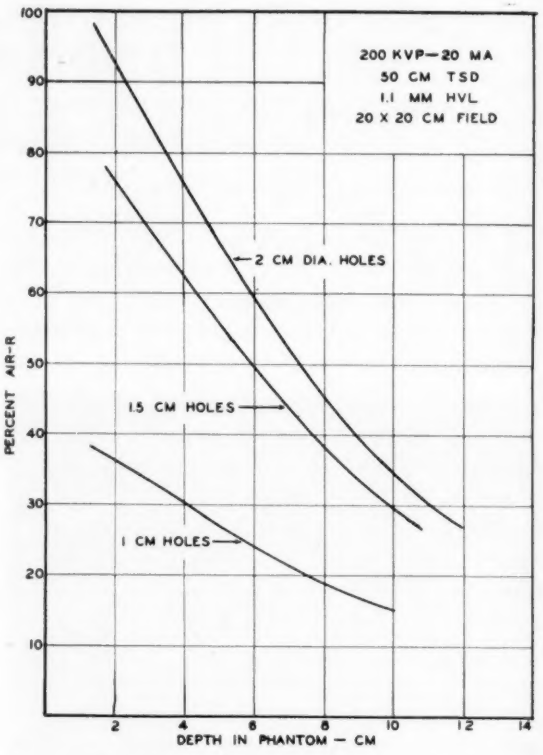

FIG. 2. Preliminary depth dose readings varying grid port size.

Grids were constructed using approximately 1.0, 1.5, and 2.0 cm. diameter holes, and depth dose measurements were made in the central ray, under the grid holes. Figure 2 shows the results of these initial readings, made with the Victoreen chamber. It was felt by the Medical Staff that the 1.5 cm. diameter hole represented the optimum port, taking into consideration the per cent depth dose delivered and the skin damage associated with the treatment.

Initial measurements were made on a 20 by 20 cm. grid of 1.5 cm. diameter holes, under the hole openings and under the lead. It soon became apparent that the Victoreen chamber was too large to detect the beam discontinuities, and involved too laborious

a procedure to make many readings. To detect the beam discontinuities,[4] a small ionization chamber probe was designed and built to facilitate rapid measurements, and a rate meter built to measure the probe current. These developments represented many man-hours of work but were worth the effort required, since they assured valid measurements and facilitated the taking of more than three thousand dosage readings.

PART I. METHOD OF MEASUREMENT OF RADIATION INTENSITY

The measurements described in this paper were made with an ionization chamber probe and dosage meter specially designed for the purpose. Unlike the method commonly used in calibrating radiation therapy machines, a rate meter was employed. The ionization chamber current was measured directly by an electrometer instrument, with a constant ion collecting voltage applied to the chamber. This procedure permits one to obtain an accurate indication of dosage rate at a given phantom location in less than two seconds. Also, if the probe can be positioned remotely, consecutive readings can be taken rapidly, and without shutting off the machine between readings. Thus, more rapid measurements are possible, facilitating more readings with a minimum of wear and tear on the roentgen-ray machine.

The electrometer instrument employed has proved to be very consistent and reliable in operation. While a full discussion of its design is beyond the scope of this paper,* the following may be of interest. The instrument is very light and compact, and operates from a 115 volt A.C. supply, rather than batteries. Unlike many electrometer instruments, this one employs negative feedback. As a result, very rapid readings are obtainable despite the use of a long cable between the probe and instrument. Also, the instrument span is relatively independent of the cable characteristics.

* A separate paper describing this instrument is now in preparation.

The probe design problem is rendered basically more difficult in this application by the necessity for a very tiny probe diameter. For example, the grid used in these measurements had holes only 5.7 millimeters apart, edge to edge. Therefore, it was felt the probe should be at most 2 to 3 mm. in diameter for proper evaluation of the radiation in the center of the lead shadow. It will be noted that this location receives the smallest tumor dose. It would hence appear that the accurate knowledge of this quantity is of considerable importance if a tumor is to be treated adequately.

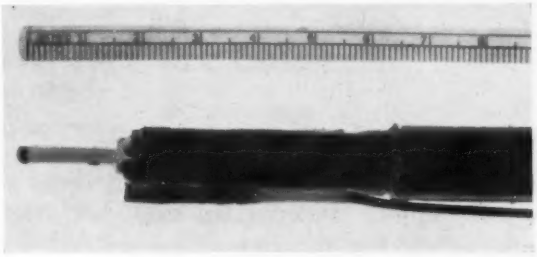

Fig. 3. Photograph of ionization chamber probe.

As a compromise between precision of sampling and practicality of construction a diameter of 2 mm. was chosen. While excellent probes have been described previously[3,4,7] this probe is the smallest possessing sufficient frequency linearity for depth dose work, to our knowledge. Figure 3 is a photograph of the probe.

Figure 4 shows an axial section view of the ionization chamber used in these measurements. The base is a turned polystyrene rod, with a 0.015 inch diameter hole in the end to hold a 0.010 inch diameter aluminum collecting electrode. The surface from which the wire emerges is heated to 50°C. and then coated with ceresin wax, for insulation. The chamber voltage (45 volts) is brought by means of an aluminum wire to the aquadag (colloidal graphite) coating on the inner surface of the sleeve, which mounts over the end of the polystyrene rod. The sleeve itself is made of cardboard, cut from a clean file card. After coating with aquadag and connecting the lead wire, the

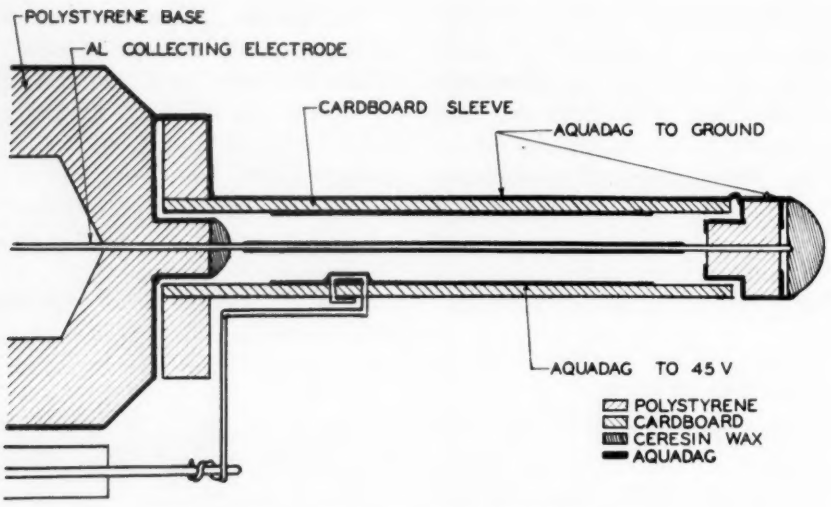

FIG. 4. Axial section view of ionization chamber probe.

sleeve is cut to size, rolled by hand about a small drill of appropriate size, and the edges glued together in overlapping fashion with polystyrene "Q-dope." The sleeve is then glued at one end to a small washer of polystyrene to assure alignment of the sleeve and polystyrene rod. A turned polystyrene cap with a 0.015 inch center hole fits over the end of the sleeve, providing a rigid mechanical mounting for the end of the aluminum collecting electrode. After the unit is glued together with "Q-dope," the protruding wire is cut short and the end sealed with ceresin wax.

The necessity for a compact probe results in considerable constructional complication. In addition, however, the problem of electrical insulation is also made more difficult. One obvious reason is that it is always more difficult to insulate conductors from each other when they are close together than when they are far apart. In addition, a small probe will produce far less ionization current than a larger one, for the same dosage rate. For example, for the same active length, a probe 8 mm. in diameter has roughly 16 times the air volume of a 2 mm. probe, since the volume varies as the square of the probe diameter. Thus, the large probe produces 16 times as much signal current, for the same dosage rate. As a result, a given amount of leakage current results in a spurious dosage rate indication 16 times greater with the small probe than with the large.

The magnitude of the leakage problem is indicated by the following illustration. For the probe used in these measurements, the useful chamber volume is only 0.03 cc. At 10 cm. depth, about 15 r per minute has been observed, producing a signal current of only 2.6 micromicroamperes (2.6×10^{-12} amperes). Under these conditions, a leakage resistance of 45 million-million ohms between collecting and outer electrode (with 45 volt chamber supply) would yield a spurious indication of 6 r per minute or 40 per cent of the dosage measured. It is seen that special insulation procedures are needed to assure accuracy of probe readings.

To reduce spurious currents across the probe to negligible values, guard rings have been employed at both ends of the cardboard tube (see Fig. 4). These rings consist of an aquadag (colloidal carbon in toluene base) coating, which is connected to electrical ground. The action of the rings is to pass any spurious or leakage current around the collecting electrode to ground; true ion current is not so by-passed, since it travels directly across the chamber volume, rather than across the surface. This construction resulted in very stable and reproducible

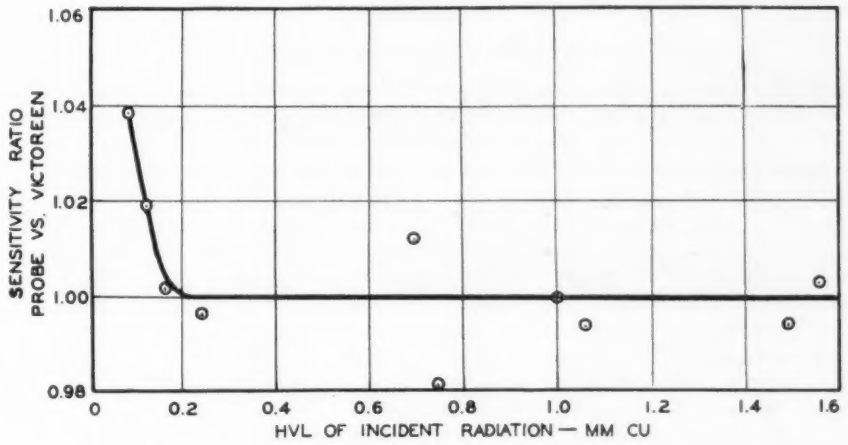

Fig. 5. Curve showing relative sensitivity of probe and Victoreen 25 r horn chamber, plotted vs. half-value layer of radiation.

operation of the probe during prolonged periods of very hot and humid summer weather.

As a further precaution against leakage, polystyrene parts were baked at 50° C. for twenty-four hours, and critical portions coated with filtered ceresin wax immediately upon removal from the oven.

In all depth dose measurements, both direct and scattered radiation must be measured. As a result, all such measurements require that the ionization chamber employed be of substantially constant sensitivity to roentgen radiation over a wide range of wavelengths. In the measurement of grid dosage, this chamber requirement is made more serious because under the lead rubber shadow almost all the tumor dosage is due to scattered radiation. Since the radiation in this shadow is softer than that found without a grid at the same depth, it is extremely important to have a good chamber linearity, particularly for longer wavelength radiation.

Among the causes of nonlinearity of "air wall" ionization chambers are the following:

(a) Absorption of longer wavelengths by the chamber wall.

(b) Absorption of electrons by the chamber wall which in free air would migrate freely between inside and outside the chamber.

(c) Production of photoelectrons at longer wavelengths, due to higher atomic number materials (metals, primarily) in the chamber wall and collecting electrode.

The use of a thin cardboard tube for the wall of the ionization chamber reduced both (a) and (b) above. The photoelectric effect is more difficult to control. To solve this problem, all metal parts in the probe volume were coated with aquadag to an estimated 0.003 inch thickness. As a result of this treatment, most photoelectrons emitted by the aluminum wires are absorbed, while those few escaping are sharply reduced in speed and hence in ability to produce ionization.

To verify the linearity of the chamber used in these measurements, roentgen radiation of half-value layer from 0.1 mm. to 1.5 mm. of copper was used. Comparison was made with a 25 r Victoreen horn chamber. Figure 5 shows a curve in which is plotted the ratio of probe reading in arbitrary meter units to r per minute measured with the Victoreen chamber as a function of half-value layer of incident radiation. The ratio at half-value layer = 1.0 mm. Cu is taken as unity. It will be observed that the probe reads up to 4 per cent higher than the Victoreen chamber for softer radiation. This is perhaps due to the thinness of the wall of the small probe, which assures sensitive response to radiation beyond the

TABLE II

ROENTGENS AT DEPTH PER 100 R IN AIR

Half-value layer = 1.10 mm. Cu (200 kv.p. Villard, 0.5 mm. Cu plus 1 mm. Al filter)
Grid: 1.0 mm. Pb equivalent; 46 per cent opening, 1.43 cm. diameter holes.
Target-grid distance, 50 cm.

Field Size	20×20 cm. (Bakelite cover)		15×15 cm. (No cover)		10×10 cm. (No cover)	
Depth cm.	Hole	Lead	Hole	Lead	Hole	Lead
0	112	26	115	26	109	22
2	94	35	98	33	92	28
3	83	36	85	34	79	28
4	72	36	73	33	67	27
5	62	35	62	31	57	25
6	54	32	53	29	48	23
7	46	29	46	27	41	22
8	40	26	40	25	35	20
10	31	22	30	20	25	15
12	23	17	22	16	18	12
14	17	13	16	12	13	9
16	13	10	12	10	9	7
20	7	5	6	5	5	4

wavelength range of the horn chamber. The good agreement of the two chambers and the general acceptance of the Victoreen chamber for depth dose measurements lead to the conclusion that the small chamber is of useful accuracy for the measurements intended.

In employing the probe for depth dose measurements, a masonite phantom was used. To assure a sufficiently small air space between the probe and the phantom, the cardboard tube was inserted into a carefully machined cap. This was removable, with care, for air dose measurements, but was left in place for depth dose measurements. The cap material was purple heart wood, which tested at substantially unity specific gravity. Normally the cap is kept over the chamber for protection, assuring a rugged unit under storage conditions.

The air volume of the probe is substantially annular, and therefore highly symmetric. One would hence expect reasonable independence of sensitivity from voltage supplied to the chamber. No measurable change in reading is observed when the probe voltage is varied from 25 to 150 volts. A voltage of 45 volts is normally used.

PART II. EXPERIMENTAL RESULTS

In order to present data in a form most useful to the clinical radiologist depth dose in this paper is expressed as dose at depth for 100 r in air. Data were obtained using a 200 kv. (peak), 20 ma. Villard circuit generator, with a target-grid distance of 50 cm. The grid used was of 1 mm. lead equivalent lead rubber. It had a 46 per cent exposure and 1.43 cm. diameter holes, as previously described.

Tables II and III present data measured beneath the central ray, both directly under the grid hole and under the adjacent lead shadow. They show the number of roentgens received at various depths for every 100 r delivered in air. In Table II, 0.5 mm. Cu plus 1 mm. Al filter was used; in Table III, 1 mm. Cu plus 1 mm. Al filter. In both tables, field sizes of 20 by 20, 15 by 15, and 10 by 10 cm. are included.

Figures 6, 7, and 8 show the same information as that included in Tables II and III, in graphical form. The upper curves show data taken under the central hole; the lower curves, data taken under the adjacent lead shadow. The curves show graphically how the radiation intensity

TABLE III

ROENTGENS AT DEPTH PER 100 R IN AIR

Half-value layer = 1.82 mm. Cu (200 kv.p. Villard, 1 mm. Cu plus 1 mm. Al filter)
Grid: 1.0 mm. Pb equivalent; 46 per cent grid, 1.43 cm. diameter holes.
Target-grid distance = 50 cm.

Field Size	20×20 cm. (Bakelite cover)		15×15 cm. (No cover)		10×10 cm. (No cover)	
Depth cm.	Hole	Lead	Hole	Lead	Hole	Lead
0	114	29	117	27	111	24
2	97	37	100	37	95	29
3	86	38	88	38	81	28
4	75	37	76	37	69	27
5	65	36	65	34	59	25
6	57	33	56	31	50	23
7	49	30	48	28	43	22
8	43	27	42	25	37	20
10	33	23	32	20	27	15
12	25	18	24	16	20	12
14	19	14	18	12	14	9
16	14	11	13	10	10	7
20	8	6	7	5	5	4

smooths out as the tumor depth is increased.

Table IV shows the ratio of the radiation received under the hole to that received under the adjacent lead, for both 0.5 mm. and 1 mm. Cu filter, and three field sizes. It is easily seen that the ratio of these two intensities approaches unity as the depth increases, with the skin under the hole receiving about 4 times the amount of radia-

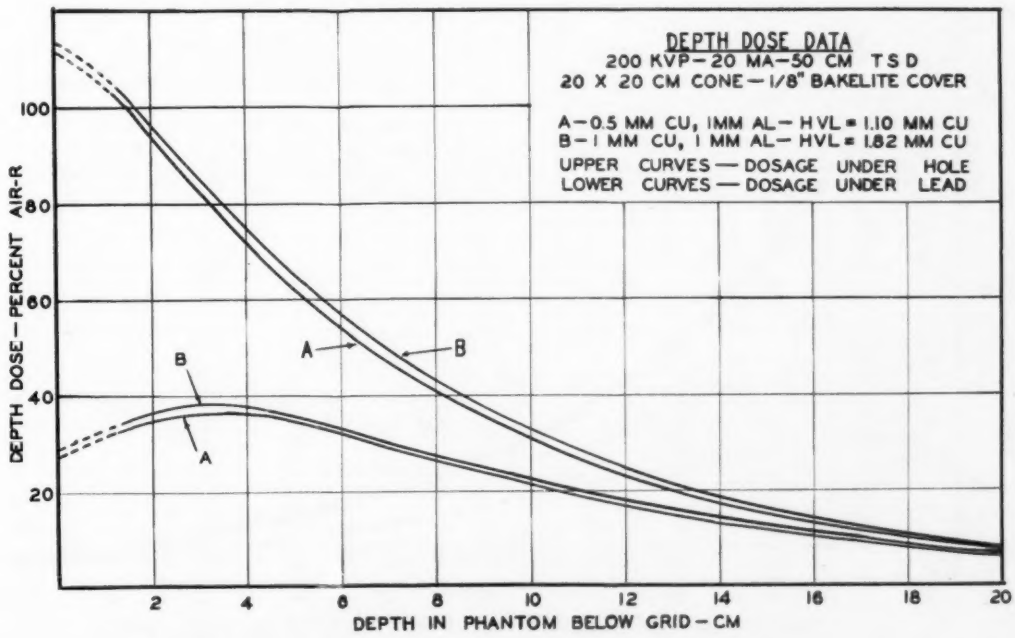

FIG. 6. Dose at depth per 100 r in air vs. depth in cm.; 20 by 20 cm. cone with bakelite cover.

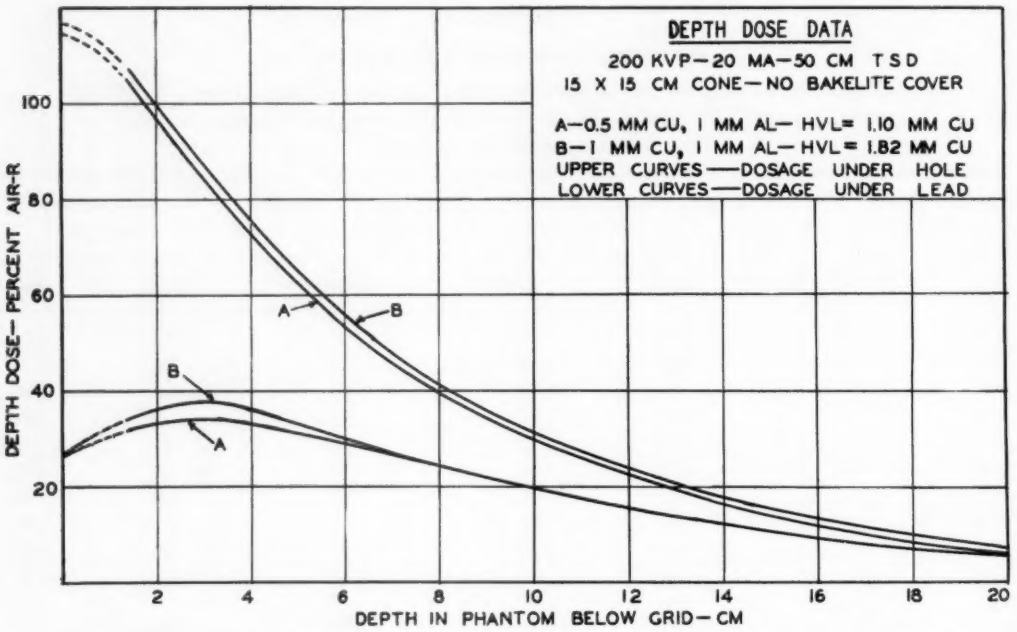

FIG. 7. Dose at depth per 100 r in air vs. depth in cm.; 15 by 15 cm. cone, without cover.

tion compared to that under the lead. At 10 cm. depth, the ratio lies between 1.4 and 1.8. The objection has been raised that grid technique would undertreat portions of the tumor. This is a reasonable objection, but it can be partially overcome by angulation of the tube (of the order of 5° for most cases), and a more even dose thereby delivered at 10 cm. However, when doing this, allowances must be made for the increased target-skin distance, if any. When angling the tube, account should also be

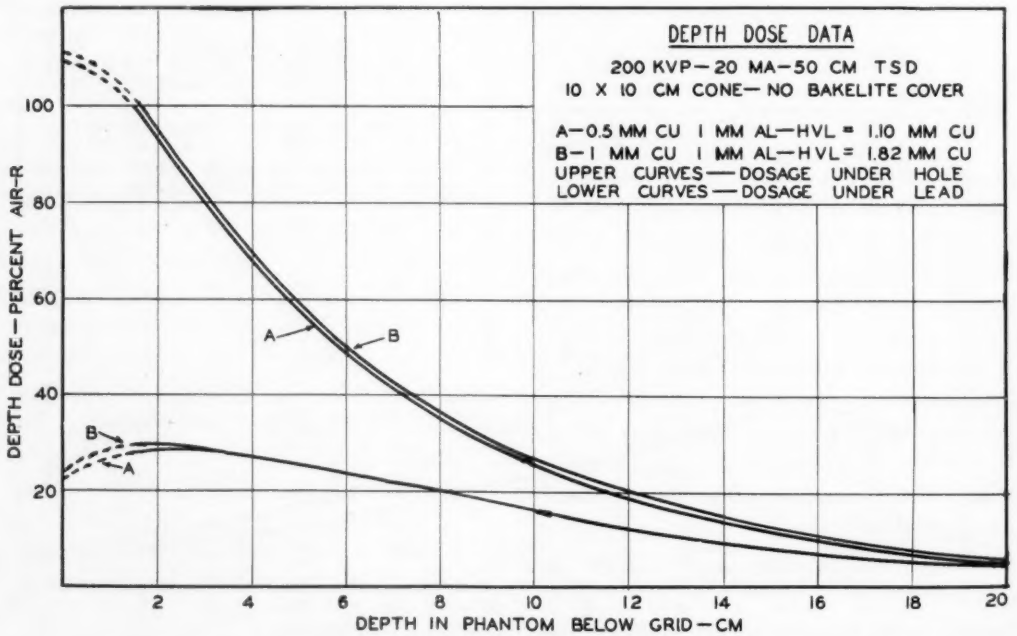

FIG. 8. Dose at depth per 100 r in air vs. depth in cm.; 10 by 10 cm. cone, without cover.

Table IV

RATIO OF INTENSITY UNDER CENTRAL HOLE TO INTENSITY UNDER LEAD

Field Size / Depth cm.	20×20 cm. (Bakelite cover)		15×15 cm. (No cover)		10×10 cm. (No cover)	
	0.5 mm. Cu	1 mm. Cu	0.5 mm. Cu	1 mm. Cu	0.5 mm. Cu	1 mm. Cu
0	4.3	3.9	4.4	4.3	4.9	4.6
2	2.6	2.6	3.0	2.7	3.3	3.8
4	2.0	2.0	2.2	2.0	2.5	2.55
6	1.7	1.7	1.8	1.8	2.1	2.2
8	1.5	1.6	1.6	1.7	1.8	1.85
10	1.4	1.4	1.5	1.6	1.7	1.8
12	1.35	1.4	1.4	1.5	1.5	1.7
14	1.3	1.4	1.3	1.5	1.4	1.6
16	1.3	1.3	1.2	1.3	1.3	1.4
20	1.3	1.3	1.2	1.4	1.25	1.25

taken of how much dosage the total tumor receives in the grid shadow as it is moved, since this represents the minimum tumor dose.

To determine the extent of variation of intensity at a given depth under the grid, measurements were made as follows:

1. Measurements were made every millimeter at the 1.5 cm., 5.5 cm. and 10.5 cm. depths. These were plotted carefully and the shape of the "hills and valleys" studied.

2. At all other levels in the phantom, readings were made at the maximum and minimum intensities.

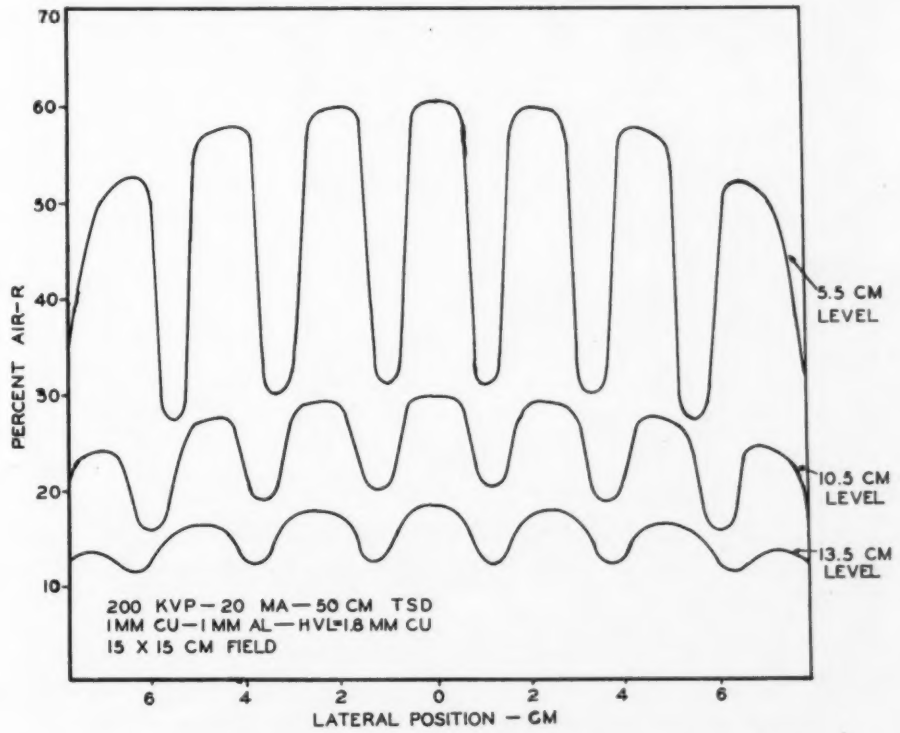

Fig. 9. Dose at depth per 100 r in air vs. lateral position at 5, 10 and 15 cm. depth; 15 by 15 cm. cone.

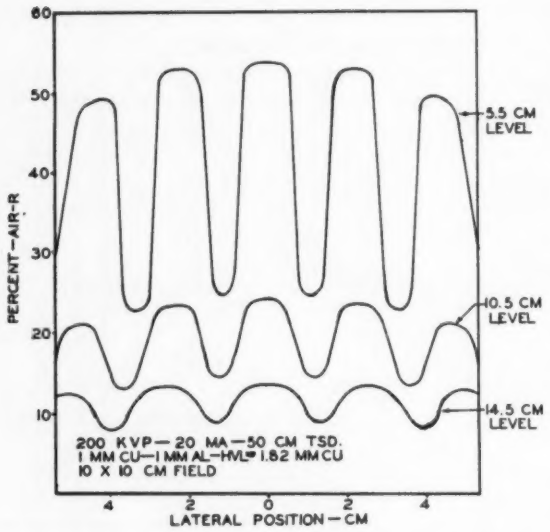

FIG. 10. Dose at depth per 100 r in air vs. lateral position at 5, 10 and 15 cm. depth; 10 by 10 cm. cone.

The results of No. 1 above are presented as isodepth curves for 10 by 10 and 15 by 15 cm. cones (see Fig. 9 and 10). Also included (Fig. 11) is the complex isodose curve for a 20 by 20 cm. cone, bakelite covered, for 200 kv. (peak), half-value layer = 1.82 mm. of copper. Target-grid distance 50 cm., filter = 1 mm. Cu and 1 mm. Al. The isodose curve was derived by combining measurements 1 and 2 above. The actual shape of the isodose lines was inferred from measurements 1. These figures represent intensities across the field at right angles to the tube axis.

The question is frequently asked, "What does the skin receive under the lead?" To evaluates skin dose, measurements were made with the small ionization chamber buried in the phantom in such a manner that the center electrode was at the level of the skin. The grid was placed over the

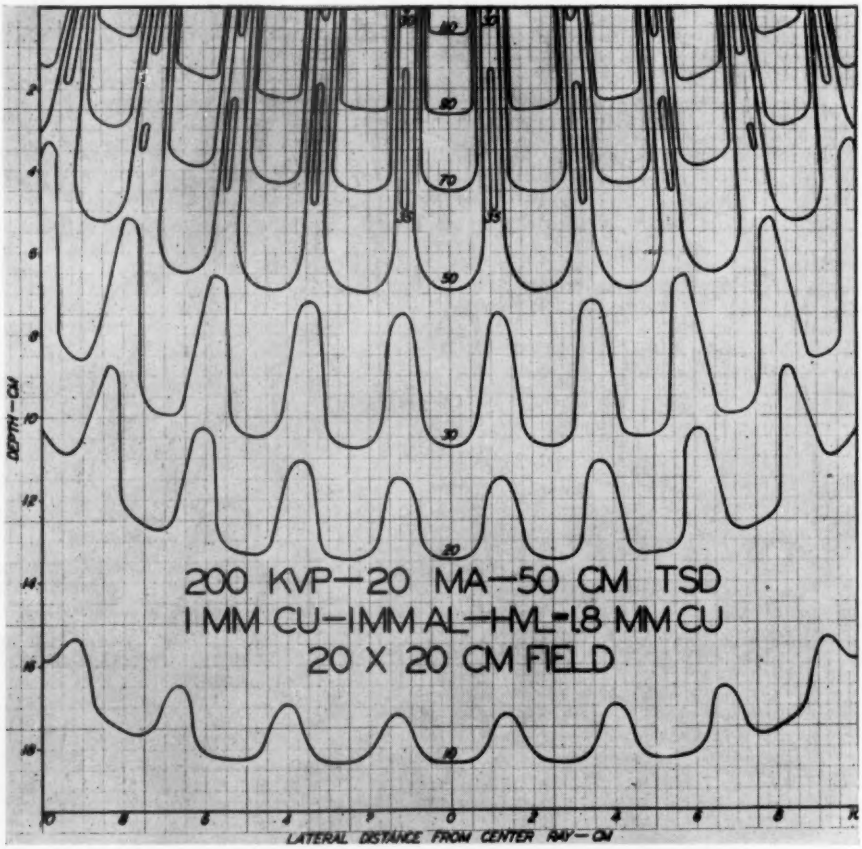

FIG. 11. Isodose curve for 20 by 20 cm. cone (bakelite cover).

chamber and measurements made under a hole and under the adjacent lead rubber. It was realized that the lead rubber is raised a distance off the surface of the phantom equal to the radius of the chamber; for this reason, these points are plotted on the curves and connected to the rest of the curve with dotted lines in Figures 6, 7 and 8. It is of interest to note the comparison of our data with previous literature.

Jolles[5] states that the amount of scattered radiation received from a small port to an adjacent area never exceeds 6 per cent, and is less than 2 per cent for separations above 3 cm. In the case of a grid, an area under the lead is surrounded by 4 adjacent ports. This, then, would give us about 24 per cent under the lead from scattering. Inasmuch as 1 mm. of lead will transmit about 7 per cent the total radiation received under the lead would be 31 per cent. Our measurements indicate the right order of magnitude for skin dose, and since there are actually more than 4 ports around a leaded area, this theoretical value is probably low. However, since round holes are used instead of square ones, it is reasonable to expect the measured value to be somewhat lower than 31 per cent. Actually in the order of 29 per cent was measured. All in all, it seems that the skin dose as measured is of a reasonable value. If, at a later date, a small extrapolation chamber is developed, the results will be made available.

More studies can be made using different sized holes, thicker lead rubber, and different per cent exposures. In fact, the number of possible combinations is probably infinite. But from the physics involved and the clinical results it is felt that this is an optimum range in which to work. Further work along these lines is indicated, but these data may help the radiologist without a multimillion volt roentgen-ray unit to obtain the depth dose in which he is interested. It is sincerely hoped that these data will be useful to radiologists, and from the requests made of the authors for such data, it is felt that this study will be useful.

SUMMARY

Depth dose data for a lead rubber grid are presented for three cone sizes. Both curves and tables are presented as a guide for therapists, and a complete depth dose diagram shown.

A brief outline is given of the design and application of grids for grid therapy.

To validate the readings, a fairly complete discussion of a special tiny ionization chamber probe developed for measuring depth dose below the grid is included.

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We wish to thank Dr. B. P. Widmann and the members of the Department of Radiology for their encouragement and criticisms during this work. We extend our appreciation to Mr. Wayne Meyers and Mr. Gottfried Buss for their assistance during the many hours of data recording, and to Mr. Charles K. Simpson for his skillful machining of delicate probe components.

REFERENCES

1. Glasser, O., Quimby, E. H., Taylor, L. S., and Weatherwax, J. L. Physical Foundations of Radiology. Paul B. Hoeber, Inc., New York, 1944, p. 224.
2. Grynkraut, B. Direct and indirect radiotherapy. Am. J. Roentgenol. & Rad. Therapy, 1945, *53*, 491–499.
3. Herbert, R. J. Negative feed-back dosage-rate meter. *Brit. J. Radiol.*, 1948, *21*, 420–424.
4. Johns, H. E., and Darby, E. K. Distribution of radiation near geometrical edge of x-ray beam. *Brit. J. Radiol.*, 1950, *23*, 193–197.
5. Jolles, B. Reciprocal vicinity effect of irradiated tissues on "diffusible substance" in irradiated tissues. *Brit. J. Radiol.*, 1950, *23*, 18–24.
6. Marks, H. New approach to roentgen therapy of cancer with use of grid. *J. Mt. Sinai Hosp.*, 1950, *17*, 46–48.
7. Turner, R. C., and Newberry, S. P. Probe type direct reading dosage-rate meter. *Brit. J. Radiol.*, 1950, *23*, 424–429.

THE DIAGNOSTIC VALUE OF THE IMMEDIATE PERIPHERAL LEUKOCYTE RESPONSE OF THE RAT TO WHOLE BODY ROENTGEN IRRADIATION*

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IN THE reports of LeRoy[6] and Liebow, Warren and DeCoursey[7] on the clinical and pathological data of the atomic bomb casualties at Hiroshima and Nagasaki, a great void was noted in the knowledge of early postirradiative changes in the hemopoietic system. Of the extensive experimental work done in this field, little has been detailed concerning the leukocyte response in the immediate postirradiation period. This report concerns itself primarily with the changes in the peripheral white blood cells in *the same animal* from hour to hour *immediately* after whole body roentgen irradiation, in order to determine the lethality of various levels of roentgen-ray exposure.

EXPERIMENTAL

Wistar white rats, each weighing approximately 200 grams, were irradiated with the following roentgen-ray factors: 200 kv., 25 ma., 50 cm. distance, 68 r/min., half-value layer 1.1 mm. Cu, obtained with 0.5 mm. Cu and 1.0 mm. Al filter. The rats were immobilized without anesthesia during treatment in close fitting compartments of a thin-walled wooden box. They were divided into eight groups of 2 to 4 animals each and given irradiation in doses from 85 r to 5,000 r.

The white blood cell and differential counts were done immediately before irradiation and then once hourly around the clock for twenty-four hours. Counts then were done on each successive day for two weeks and once weekly for the following two weeks. Blood was obtained by puncturing the tail vein and all counts were done by the same technicians. The rats in the control group were given a sham treatment. The blood counts in this as in all other groups were carried out under similar circumstances.

RESULTS

In the control group (Fig. 1), the lymphocyte count of the normal rat is higher than the leukocyte count, and this relationship is not disturbed by the hourly and daily sampling extended over a period of four weeks. A transient drop in the white blood cell count due to a mild lymphopenia is noted for about fourteen hours after the sham treatment. This is followed by a slight rise in the white blood cell count due chiefly to a lymphocytosis which persists to the twelfth day. Neither the initial lymphopenia nor subsequent lymphocytosis is very marked. At no time does the curve of the lymphocyte cross the curve of the leukocyte count, both curves maintaining their relationship throughout the experimental period in spite of anemia which doubtlessly was present as the result of repeated bleeding incident to the numerous blood counts.

In Group II, rats irradiated with 85 r (Fig. 2), an initial drop in the lymphocyte count occurs as in the control group, but by the twelfth hour the drop carries the lymphocyte curve downward below the curve of the leukocyte count which in turn shows four sharp rising peaks at the sixteenth and twenty-first hours, and again on the second and fifth days. A normal lymphocyte count replaces the lymphopenia at the twenty-first hour with secondary rises on the second and fifth days. The lymphocyte curve returns to a relatively normal position on the second day, after which all counts tend to rise from a depressed to almost normal levels by the fourth week.

In Group III, rats irradiated with 175 r (Fig. 3), an initial drop in the lymphocyte count occurs within four hours, crossing the rising leukocyte count earlier than with the smaller dose in the previous group. At the ninth hour, the first of several intermittent elevations in the leukocyte curves occurs, to be followed by progres-

* Funds of the Louis Sitnek Trust of the Eagleville Sanatorium, Eagleville, Pennsylvania, partially defrayed expenses of these studies.

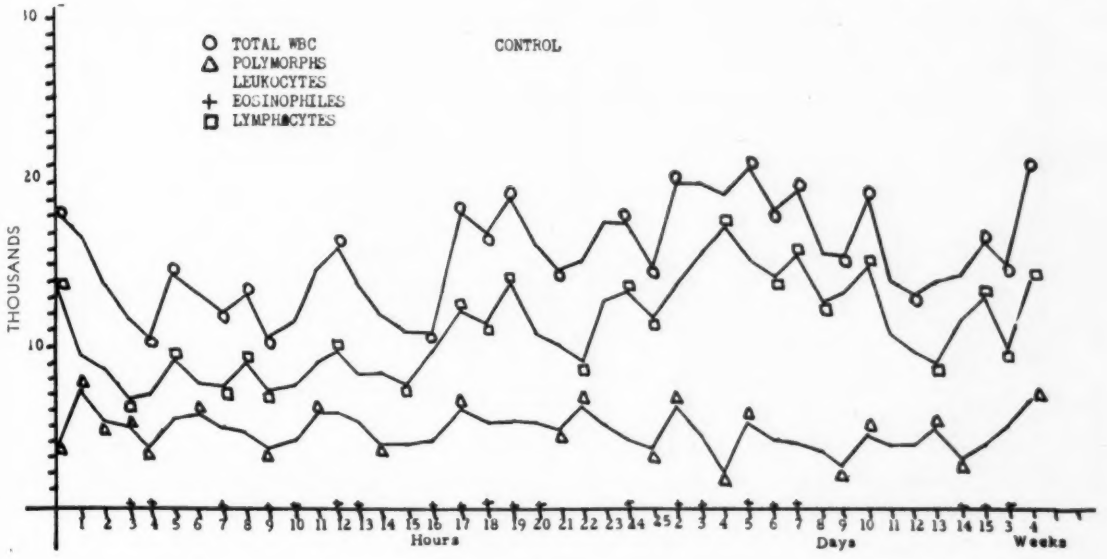

Fig. 1

sively greater rises at the fifteenth and twentieth hours, when the highest peak of 42,000 is reached. Another secondary rise occurs at the twenty-fourth hour. Meanwhile, the lymphopenia persists during the entire twenty-four hour period and does not return to normal until the fifth day. Thereafter, all counts remain slightly below normal, although relatively oriented.

In Group IV, rats irradiated with 350 r (Fig. 4), a sharp drop in the lymphocyte count again occurs within four hours, followed by a less precipitous decline during the next four hours, remaining thus depressed in the region of 1,000

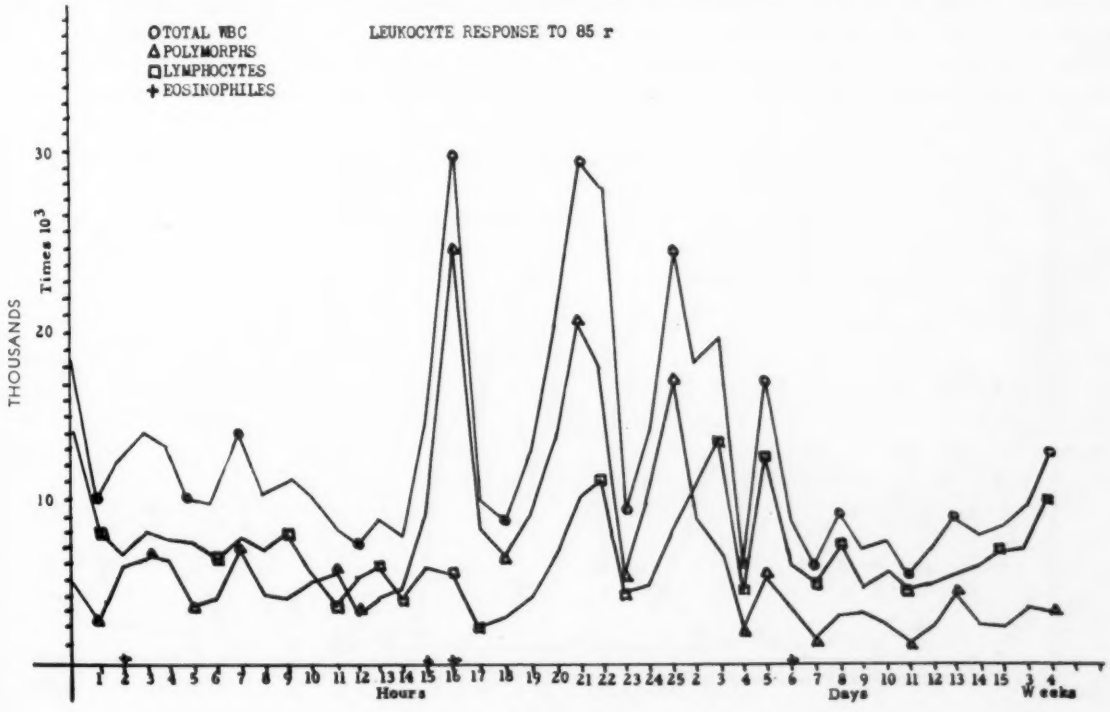

Fig. 2

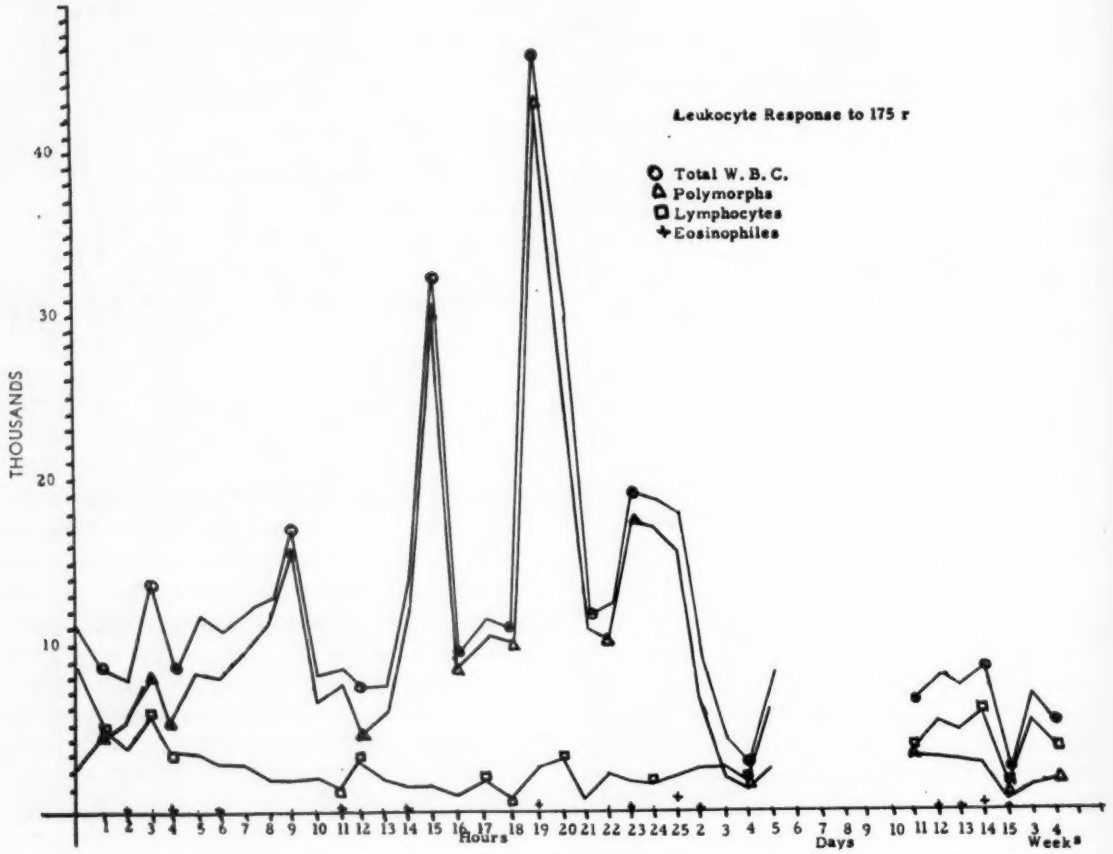
Leukocyte Response to 175 r
Total W. B. C.
Polymorphs
Lymphocytes
Eosinophiles
THOUSANDS
40
30
20
10
Hours
Days
Weeks

FIG. 3

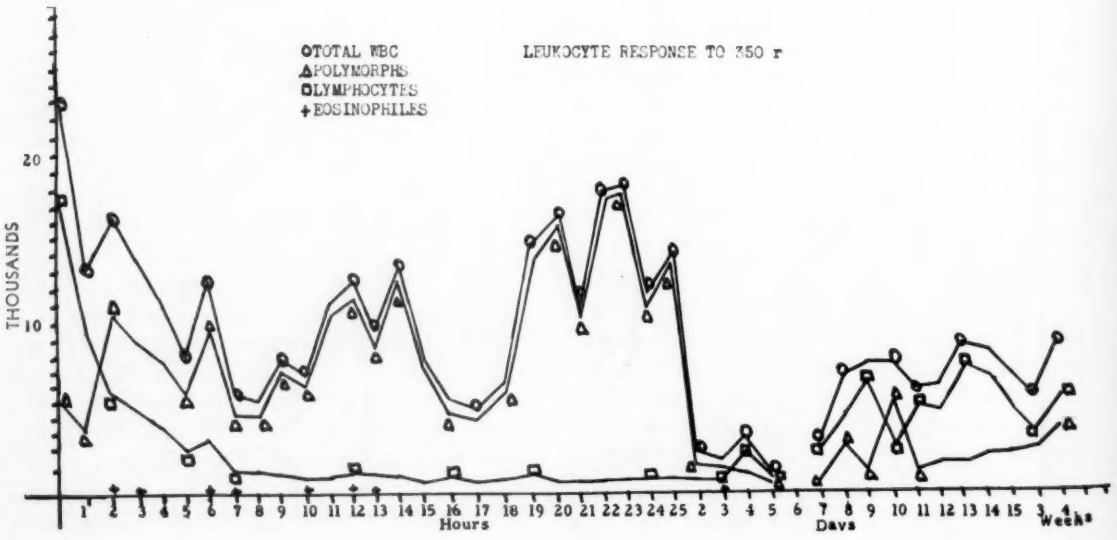
TOTAL WBC
POLYMORPHS
LYMPHOCYTES
EOSINOPHILES
LEUKOCYTE RESPONSE TO 350 r
THOUSANDS
20
10
Hours
Days
Weeks

FIG. 4

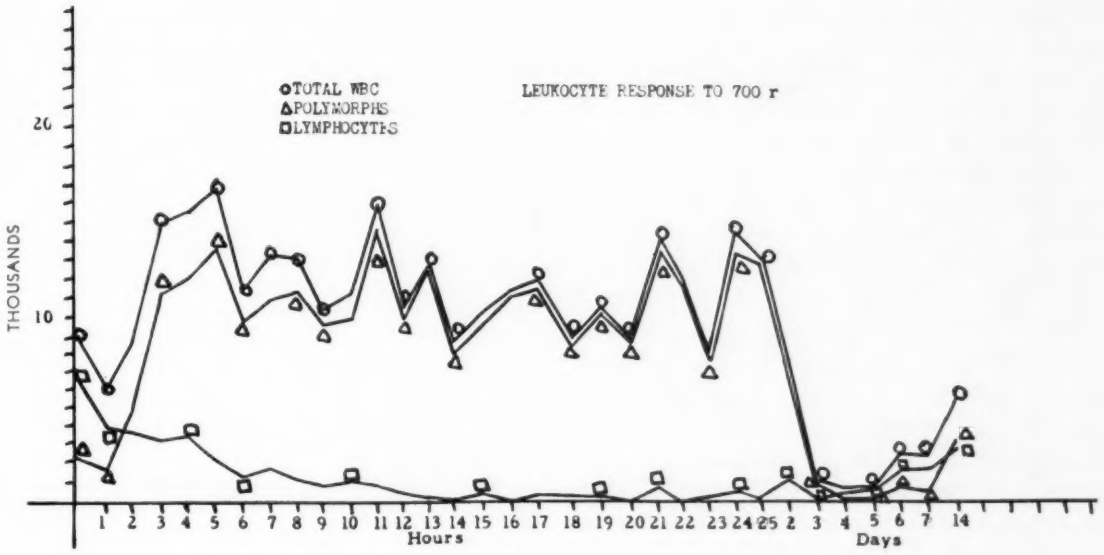
TOTAL WBC
POLYMORPHS
LYMPHOCYTES
LEUKOCYTE RESPONSE TO 700 r
THOUSANDS
20
10
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 2 3 4 5 6 7 14
Hours
Days

FIG. 5

per cu. mm. until about the eighth day, when the curve begins to ascend. The curve of the polymorphonuclear counts crosses that of the lymphocytes at the second hour. A slightly greater elevation of the leukocyte count occurs at the twelfth hour, and again with still greater intensity at the nineteenth and twenty-second hours. At the end of forty-eight hours, a sharp drop in the leukocyte count occurs and for the succeeding six days both a lymphopenia and leukopenia persists. This abnormal state is gradually corrected during the following three weeks, but entirely normal elevations are not quite reached even at the end of four weeks.

In Group v, rats irradiated with 700 r (Fig. 5), a dose regarded generally as mid-lethal during a thirty day period, the lymphocyte curve turns sharply downward during the first four hours, reaching its lowest level of approximately 600 per cu. mm. at the twelfth hour. This level is maintained for about two weeks before ascending, and its general appearance is not much

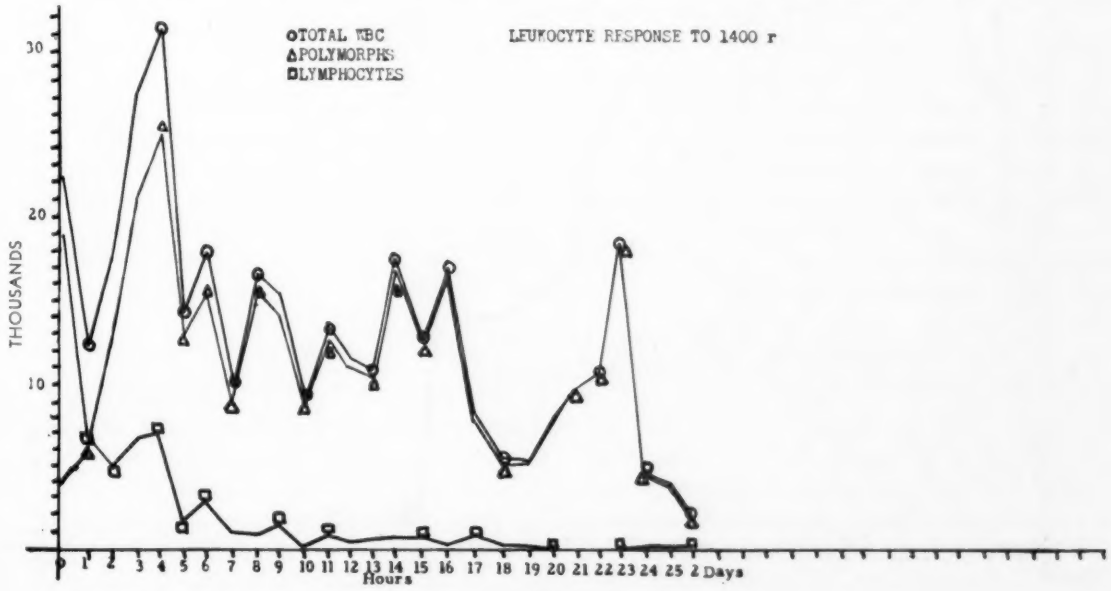
TOTAL WBC
POLYMORPHS
LYMPHOCYTES
LEUKOCYTE RESPONSE TO 1400 r
THOUSANDS
30
20
10
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 2 Days
Hours

FIG. 6

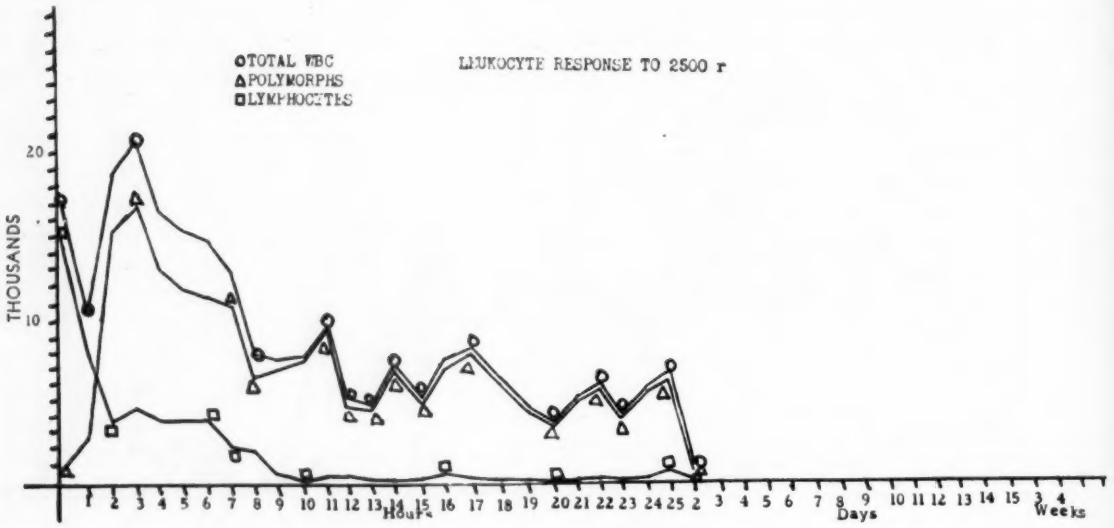
OTOTAL WBC
ΔPOLYMORPHS
□LYMPHOCITES
LEUKOCYTE RESPONSE TO 2500 r
THOUSANDS
20
10
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 2 3 4 5 6 7 8 9 10 11 12 13 14 15 3 4
Hours
Days
Weeks

FIG. 7

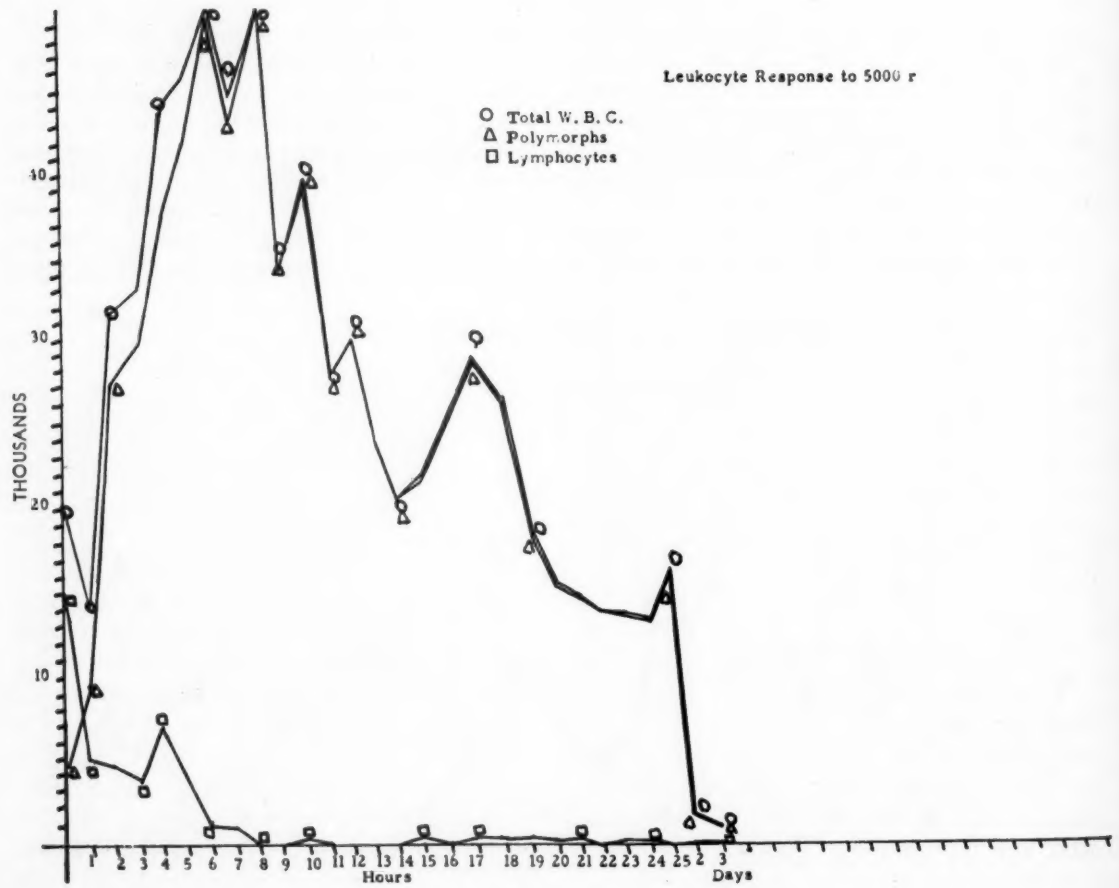
Leukocyte Response to 5000 r
O Total W. B. C.
Δ Polymorphs
□ Lymphocytes
THOUSANDS
40
30
20
10
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 2 3
Hours
Days

FIG. 8

different from that in Group IV, where only half the roentgen-ray dose (350 r) was used.

The leukocyte curve ascends sharply during the first three hours, crossing that of the lymphocyte count at the end of one hour. Thereafter, intermittent elevations occur approximately at three hour intervals until a precipitous fall takes place on the third day. A combined lymphopenia and leukopenia then persists until about the fourteenth day.

In Group VI, rats irradiated with 1,400 r, a dose greater than lethal (Fig. 6), a precipitous drop in the curve of the lymphocyte counts occurs during the first two hours, and at the sixteenth hour the counts drop below 500 per cu. mm. These low counts persist until death on the second or third day. The leukocyte curve rises steeply during the first four hours, reaching a level greater than 30,000 per cu. mm. It then drops with progressively lower intermittent elevations. A marked leukopenia occurs on the second day, having been preceded by one last temporary elevation at the end of the first day.

In Group VII, rats irradiated with 2,500 r (Fig. 7), the pattern of white blood cell curves is similar to those in Group VI. After the initial leukocytosis which occurs about the fourth hour, the ensuing leukopenia is greater and is interrupted with less intense intermittent elevations than in the previous group.

In Group VIII, rats irradiated with 5,000 r (Fig. 8), not only does the lymphocyte curve take a very rapid drop within the first six hours, but also the lymphopenia tends to be replaced by an almost complete absence of lymphocytes in the circulation up to the time of death. The initial leukocytosis, which occurs during the first eight hours, is very intense, rising to 50,000 per cu. mm. This is followed by an intermittent but progressive decline, reaching leukopenic levels of 1,000 per cu. mm. during the twenty-four hours preceding death on the third day.

DISCUSSION

The taking of blood samples every hour from the same rat for twenty-four hours and subsequently every day, as was done in these experiments, did not pose the difficulties of collection or clotting which we were led to anticipate. This may have been due to the fact that only enough blood was taken at each examination for a white blood cell and differential count. Approximately 0.25 milliliter of blood was taken for each hourly count so that at the end of the first day, a total of 6 ml. of blood was withdrawn. The anemia thus produced doubtlessly had an influence on the pattern of the blood curves, but the results are tabulated relatively against the control group rather than against the absolute hematologic status.

In the control group, the initial drop in the total white blood cell and lymphocyte counts, which continued for four hours, might be ascribed to the alarm reaction, but the marked and precipitous initial drops in the curves of the lymphocyte counts observed with increasing doses of radiation are probably the result of the combined nonspecific effect of the alarm reaction and the specific effect of roentgen irradiation. Ellinger[3] has long maintained that radiation sickness corresponds to the alarm reaction of Selye, being an unspecific response to body stress. With smaller nonlethal doses of whole body irradiation, the pattern of the hourly white blood cell differential counts gives support to Ellinger's point of view; but with the lethal and superlethal doses, the pattern changes entirely, doubtlessly because of the additional specific roentgen-ray effects.

While the lymphopenia is greater and longer sustained the higher the dose of radiation, the qualitative character of all the lymphocyte curves is similar. This is not true of the leukocyte curves. With the smaller doses, ranging from 85 r to 700 r, the peaks of neutrophilia occur with intermittent waves toward the end of the first day after irradiation, whereas with the lethal doses, those above 1,400 r and up to 5,000 r, the leukocytosis occurs more immediately and with greater intensity during the earlier hours of the first twenty-four hour period after irradiation. Following this, there occurs a rapid leukopenia which is marked for several hours before death on the second or third day.

In those groups of rats receiving whole body irradiation in doses less than 700 r,

the white blood cell counts tend to return toward normal levels approximately between the twelfth and sixteenth days. From the work of Kline and Cliffton,[5] who determined the life span of leukocytes in the human to be approximately 12.8 days, it is possible from our observations that rat white blood cells have a similar life span. This possibility is further suggested by the work of Brecker, Endicott, Gump and Brawner,[1] who estimated the suppression of lymphopoiesis in mice after roentgen irradiation to be about fourteen days in duration.

If in man similar immediate qualitative and quantitative differences in the neutrophil and lymphocyte counts occur with different doses of whole body irradiation within twenty-four hours after exposure, an excellent diagnostic means for effective therapy might be possible with accidental or atomic bomb warfare casualties, since many valuable therapeutic suggestions already have been made for sustaining animals after irradiation with sublethal doses, especially with exchange blood transfusions[8] and injections of splenic[4] and bone marrow extracts.[2] Larger animals, possibly including primates, might be used to good advantage for checking our results.

SUMMARY

To test whether characteristic periodic and quantitative changes in the whole and differential white blood cell counts might occur with different doses of whole body roentgen irradiation during the first twenty-four hour period after exposure, several groups of rats were studied with doses varying from 85 r to 5,000 r. It was found that:

(1) Initial progressive lymphopenia occurs during the first four hours after exposure.

(2) The larger the dose, the more precipitous is the initial drop of the curve of lymphocyte counts, and the more persistent are the low counts.

(3) Lethal doses cause lymphocyte counts below 500 per cu. mm.

(4) With doses of irradiation in the midlethal ranges, leukocytosis occurs almost simultaneously with the lymphopenia during the first few hours after irradiation.

(5) Marked differences occur, however, in the differential blood curves between sublethal and superlethal doses. In the groups receiving superlethal doses, the early marked leukocytosis succeeded by the marked combined leukopenia and lymphopenia a few hours before death are striking differences from the patterns of the white blood cell curves in those groups receiving lethal or sublethal doses of radiation. These differences may have significant diagnostic and therapeutic value.

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Philadelphia 3, Pennsylvania

Two skilled technicians merit our gratitude for their reliable assistance given in the laboratories of the Pennsylvania Eastern State Penitentiary Hospital (Dr. W. J. Tourish, Medical Director).

REFERENCES

1. BRECHER, G., ENDICOTT, K. M., GUMP, H., and BRAWNER, H. P. Effects of x-ray on lymphoid and hemopoietic tissues of albino mice. *Blood*, 1948, *3*, 1259–1274.
2. CONGDON, C. C., UPHOFF, D., and LORENZ, E. Modification of acute irradiation injury in guinea pigs by bone marrow injections. Scientific Exhibit at Meeting of American Association of Pathologists and Bacteriologists, New York City, April, 1952.
3. ELLINGER, F. Newer concepts of radiation sickness and its treatment. Lecture and Review Series No. 51–56, Naval Medical Research Institute, Bethesda, Md., May 23, 1951.
4. JACOBSON, L. O., SIMMONS, E. L., MARKS, E. K., and ELDREDGE, J. H. Recovery from radiation injury. *Science*, 1951, *113*, 510–511.
5. KLINE, D. L., and CLIFFTON, E. E. Life span of leucocytes in human. *Science*, 1952, *115*, 9–11.
6. LEROY, G. V. Hematology of atom bomb casualties. *Arch. Int. Med.*, 1950, *86*, 691–710.
7. LIEBOW, A. A., WARREN, S., and DECOURSEY, E. Pathology of atomic bomb casualties. *Am. J. Path.*, 1949, *25*, 853–1027.
8. SWISHER, S. N., and FURTH, F. W. Effect of early small exchange transfusion on x-irradiated dog. *Proc. Soc. Exper. Biol. & Med.*, 1951, *78*, 226–229.

Vol. 71, No. 5

A REVIEW OF THE THEORY, CALIBRATION TECHNIQUES, AND APPLICATIONS OF AN IONIZATION CURRENT COMPARATOR, WITH AN INVESTIGATION OF ITS CAPABILITIES AS A PRECISION INSTRUMENT*

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EARLIER papers[2,3,4,5] have given some account of the theory, design and common applications of a very simple instrument which, by a null method, enables a direct comparison to be made of the magnitudes of two ionization currents, while a later paper[6] describes an experimental method of calibration, easily performed, and capable of high accuracy. All measurements in which monitoring of roentgen-ray output by a second ionization chamber is regarded as essential can thus be carried out with great facility. Such measurements include those of percentage depth dose in a phantom, absorption measurements (including those of half-value layer), together with cross-field distributions and inverse square law deviations associated with radiation beams in air. The instrument also has possibilities as a radioactive source comparator.[2]

Since the publication of these earlier papers, which, incidentally, referred mainly to the more routine clinical applications just enumerated, the quest for high precision in new types of measurement has led to the desirability of a more detailed understanding of the behavior of the instrument, and to the need for alternative calibration procedures. In the main, these developments have been associated with the application of the comparator to free-air chamber work, but as they are also of more general applicability, a review of the present position seems desirable. We shall therefore describe below:

(a) A fuller theory of the instrument than has hitherto been published;

(b) A comparison between a theoretical and an experimental calibration, in the case of an actual instrument, providing excellent evidence of the accuracy of which the comparator is capable;

(c) New calibration procedures, of particular use in precision (*e.g.*, free-air chamber) work;

(d) A brief indication of the most recent applications of the instrument, and

(e) To complete the review, a brief reference to alternative design features specially suited to the more routine applications.

THEORY

For working details of the comparator, reference should be made to the earlier papers.[2,3] Essentially, however, it consists of two ionization chambers arranged to collect charges opposite in sign, and connected to opposite ends of a capacity potential divider, at least one component of which is variable, the junction of the two capacities being connected to a sensitive potential indicating device such as the grid of an electrometer triode or the needle of a Lindemann electrometer. A balance is obtained by adjusting the variable capacity until the junction of the two capacities remains at earth potential as the chamber charges accumulate. This condition is indicated by a null deflection of the detecting system. Suffice it to note here the essential

* Some of the work described in this paper was part of a thesis submitted for the Ph.D. degree of London University.

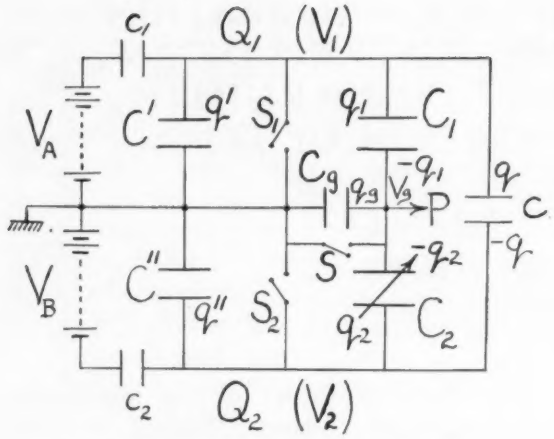

FIG. 1. Equivalent circuit of ionization current comparator.

addition to previous accounts of the theory, which is the consideration of the effects of a small stray capacity between the chamber input points of the electrometer system itself, *i.e.*, a small *capacity shunt* across the capacity potential divider. This is denoted by c in Figure 1, which depicts the equivalent circuit of the comparator. It will be shown that even when this capacity is of the order of 1 $\mu\mu$F only, it may play a significant part in the shaping of the calibration curve at one end of the instrument's range, and lead to errors of the order of 2 to 3 per cent in this region, if an attempt is made to calibrate the instrument theoretically by a method neglecting the effects of c.

Also represented in Figure 1 are the interelectrode (*i.e.*, collecting electrode to voltage electrode) chamber capacities, c_1 and c_2, the capacities to earth (C' and C'') of the inner conductors of the cables connecting the chamber collecting electrodes to the capacity potential divider (C_1 and C_2, the latter being variable). C_g, the grid-earth capacity of the electrometer triode (or the needle-earth capacity of the Lindemann) connected to the point P, is also indicated.

If, then, the total charges collected in a given time in the two chambers are $\mathcal{Q}_1$ and $\mathcal{Q}_2$ respectively (producing potentials V_1 and V_2 on the two collecting systems, and V_g at point P), charges appear in consequence on the various capacities of the system, as indicated in Figure 1. The following equations are then applicable:

$$q' = V_1 C' \quad \text{(i)}$$

$$q'' = V_2 C'' \quad \text{(ii)}$$

$$q_1 = (V_1 - V_g) C_1 \quad \text{(iii)}$$

$$q_2 = (V_2 - V_g) C_2 \quad \text{(iv)}$$

$$q_g = q_1 + q_2 \quad \text{(v)}$$

$$q_g = V_g C_g \quad \text{(vi)}$$

$$q = (V_1 - V_2) c \quad \text{(vii)}$$

$$q' + q_1 + q = \mathcal{Q}_1 \quad \text{(viii)}$$

$$q'' + q_2 - q = \mathcal{Q}_2 \quad \text{(ix)}$$

and from these it can be shown that, if V_g is to remain at zero as the charges accumulate in the chambers,

$$\left| \frac{\mathcal{Q}_1}{\mathcal{Q}_2} \right| = N,^*$$

where N may be expressed as

$$\frac{\dfrac{C_1 + C'}{C_1} + c \cdot \dfrac{C_1 + C_2}{C_1 C_2}}{\dfrac{C'' + C_2}{C_2} + c \cdot \dfrac{C_1 + C_2}{C_1 C_2}}.$$

As already noted in earlier papers, the balance condition can be satisfied by observing the anode current of the electrometer valve whose grid is connected to P (or the movement of the Lindemann electrometer needle), and adjusting C_2 until the electrometer current is restored to its initial value (or the Lindemann needle to its initial position) obtaining prior to the commencement of the accumulation of the charges, *i.e.*, prior to the opening of the three earthing keys S_1, S_2 and S. The setting of C_2 for "balance" provides the required indication of $|\mathcal{Q}_1/\mathcal{Q}_2|$, and the calibration curve relates values of $|\mathcal{Q}_1/\mathcal{Q}_2|$ to the corresponding "balance" readings on the dial attached to C_2.

CALIBRATION CONSIDERATIONS

It is clear from the above expression for N that if means are available for the accu-

* $\mathcal{Q}_1$ and $\mathcal{Q}_2$ being opposite in sign.

rate measurement of capacities in the range 0 to, say 500 $\mu\mu$F, then the calibration of the instrument can be carried out without resort to radiation. However, the measurement of small capacities to an accuracy better than 1 per cent is by no means easy, and involves the use of an expensive capacity bridge. Hence, when the comparator was first devised, it was calibrated by a direct experimental method involving the use of a roentgen-ray beam, and the application of the inverse square law.[3] More recently (as already mentioned), the much more accurate method of induced charges has been employed.[6] Nevertheless, it is very desirable to investigate the degree of agreement attainable between the theoretical and experimental calibrations, and this can be done *without* measuring the actual values of all the capacities involved. (Details of the method cannot be given here, however.) Such a comparison between theory and experiment does in fact provide a valuable indication of the accuracy of which the instrument is capable.

THE COMPARISON BETWEEN A THEORETICAL AND AN EXPERIMENTAL CALIBRATION

It has been stated above that, with circuit components as indicated and designated in Figure 1, the comparator will be balanced for a chamber charge ratio of $|\mathcal{Q}_1/\mathcal{Q}_2| = N$, where

$$N = \frac{\dfrac{C_1+C'}{C_1} + c\cdot\dfrac{C_1+C_2}{C_1C_2}}{\dfrac{C_2+C''}{C_2} + c\cdot\dfrac{C_1+C_2}{C_1C_2}}.$$

It also follows that if c, the stray capacity between the ends of the capacity potential divider, is neglected, the charge ratio for balance will be given by n, where

$$n = \frac{C_1+C'}{C_2+C''}\cdot\frac{C_2}{C_1}.*$$

* Which is the simpler balance expression given in previous papers.

The results obtained from both these expressions were therefore compared with those obtained experimentally by the method of induced charges, in the case of an actual instrument in routine use.

The dial readings at which the comparisons were made, together with the computed values of n, and the experimentally determined charge ratios for balance, are shown in Table 1. Now it is seen that the agreement between theory and experiment, using this simplified theoretical expression (n) for the balance ratio, is very good indeed (within a small fraction of 1 per cent) except at the lower end of the instrument dial, corresponding to low values of the variable component of the capacity potential divider, *i.e.*, to low values of the balance ratio. Here the deviation rises gradually to just over 2 per cent, the experimentally determined balance ratios being higher than the computed values. However, this is exactly what would be expected from a consideration of the expression for N (the more rigid theoretical value for the balance ratio), assuming that c, the stray capacity between the ends of the capacity potential divider, plays a significant part in the balance process. For, compared with n, N has the term $c\cdot(C_1+C_2)/C_1C_2$ added to both numerator and denominator, which may be expressed as $c/C_1\cdot(1+r)/r$, where $r = C_2/C_1$, the capacity potential divider ratio corresponding to the given balance position. It follows that although c is likely to be only a very small fraction* of C_1 (the fixed component of the capacity potential di vider), the factor $(1+r)/r$ will increase steadily as r decreases, *i.e.*, as the balance ratio decreases. If we assume that c is, say, approximately 0.003 C_1, then it is easily shown that the agreement between theory and experiment can be made very good indeed, even at the lower end of the calibration. That is, on this basis, *the difference between N and n at the lower end of the range (approximating to 2 per cent) closely corresponds to the discrepancy found*

* Probably less than 1 per cent.

TABLE I

Dial Reading	Experimental Charge Ratio for Balance (Induced Charge Method)	n	Percentage Deviation of n from Experimental Value	N	Percentage Deviation of N from Experimental Value
95	1.0228	1.0209	−0.19	1.0211	−0.17
90	0.9910	0.9899	−0.11	0.9901	−0.09
80	0.9243	0.9231	−0.13	0.9235	−0.09
70	0.8502	0.8495	−0.08	0.8500	−0.02
60	0.7687	0.7680	−0.09	0.7687	Nil
50	0.6792	0.6788	−0.06	0.6797	+0.07
40	0.5771	0.5766	−0.09	0.5777	+0.10
30	0.4603	0.4600	−0.07	0.4614	+0.24
25	0.3955	0.3947	−0.20	0.3962	+0.18
20	0.3259	0.3252	−0.21	0.3268	+0.28
15	0.2522	0.2507	−0.60	0.2524	+0.08
12	0.2057	0.2041	−0.78	0.2059	+0.10
10	0.1749	0.1731	−1.03	0.1750	+0.06
8	0.1448	0.1428	−1.38	0.1447	−0.07
6	0.1181	0.1158	−1.95	0.1178	−0.25
4	0.1020	0.09987	−2.06	0.1019	−0.10

to exist in practice between the value of n, and the value of the charge ratio for balance obtained experimentally by the method of induced charges.

Table I, then, gives also the computed values of N,* and it is seen that, with an average agreement approximating to 1 part in 1,000, the correlation between theory and experiment is, indeed, highly satisfactory.

In passing, it is worth noting that there is something systematic in the deviations, as they rise from almost negligible negative values to positive values of approximately 0.25 per cent, and then fall again. It is possible that this is brought about by a small but complex *variation* of c as the moving vanes of the variable component of the capacity potential divider are withdrawn from the fixed vanes.

From this investigation of the agreement between theoretical and experimental calibrations it is possible to conclude that:

(a) A very satisfactory theory of the comparator has been derived;

(b) A quick and very accurate method is available for the calibration of the comparator, the results of which are in such good agreement (almost 0.1 per cent) with theory, that the labor involved in computing the calibration is in general not justified, and

(c) The existence of a small stray capacity direct between the ends of the capacity potential divider does not significantly affect the behavior of the instrument over the majority of its range, but at the lower end of the range this capacity—even when it is very small—can be of some consequence in a theoretical calibration. It would seem desirable, therefore (although this was not done in the particular instrument studied), to *screen* the two input circuits† from one another. This is particularly true when a second (ganged) variable condenser is employed[1] to obtain a *linear* calibration.

USE OF THE COMPARATOR AS A PRECISION INSTRUMENT

As indicated above, the comparator has recently been applied to free-air chamber work, and a brief reference will be made be-

* To obtain which a value of c/C_1 (0.0029) was used which gave the best fit.

† *I.e.*, the two components of the capacity potential divider.

low to the types of measurement undertaken, or planned, in this field. It is hoped to publish a fuller account of this work in due course, but in the meantime it was felt desirable to describe as part of this review the improvements which have been made in the comparator technique as such, particularly in so far as they have enabled the inherent accuracy of the instrument to be more fully realized.

In a wide variety of experiments then, two coaxial free-air chambers have been employed, through which a narrow pencil of roentgen-rays passed in turn. The first chamber served as a comparison or monitor chamber, and the second as the experimental or measuring chamber. At first, a calibration curve drawn on a large scale* and representing the results of the induced charge method of calibration was employed, but it was eventually concluded that in the majority of the observations made, the ultimate limit to the accuracy obtainable was set by the thickness of the graph line, and the accuracy with which it could be drawn. It was therefore decided† that where the highest accuracy was required, the comparator should be calibrated point by point during the course of an experiment, as follows:

For any particular observation, the instrument is first balanced in the usual way, by adjusting the variable condenser C_2. The dial attached to C_2 is not, however, read. Instead, the circuit employed for the induced charge method of calibration is brought into play, and the *voltage ratio* E_1/E_2[6] giving a balance *at this dial setting* is found. This can be done in general with an accuracy of a few parts in 10,000, using a four-decade volt-dividing box, and errors arising from the interpolation of the comparator dial reading and associated calibration curve, or from small changes in the calibration from one occasion to another, are thus eliminated. At first the circiut

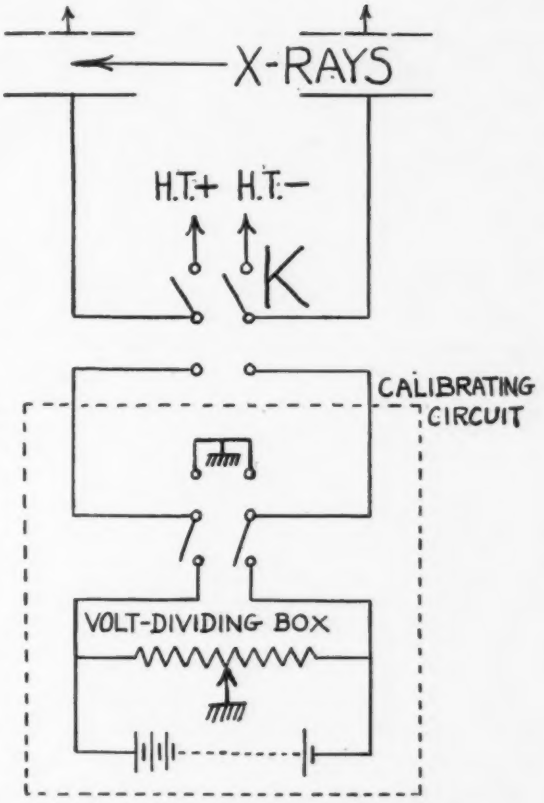

Fig. 2. Earlier circuit arrangement for point-by-point calibration in precision work.

shown in Figure 2 was employed, in which, by means of a specially constructed double-pole double-throw switch, K, the high voltage electrodes of the two chambers were disconnected from their high tension supplies, and switched over to the calibrating circuit, after each roentgen-ray balance had been obtained. In such a circuit it is the interelectrode (*i.e.*, high voltage to collecting electrode) capacities of the two chambers which are employed for the induction of the calibrating charges.[6] This arrangement is no longer possible, however, if either chamber (or both) incorporates a guard-wire system with graded potentials on it, particularly if—as is convenient—a tapped potentiometer, connected from the high voltage plate to earth, is employed to obtain these intermediate potentials. (For, among other things, it is to be noted in this connection that the presence of the guard wires—with their graded potentials—af-

* The scale lengths of the graph were 1 meter in either direction.

† Following a suggestion by my colleague Miss Sheila M. Hall, B.A., which I acknowledge gratefully.

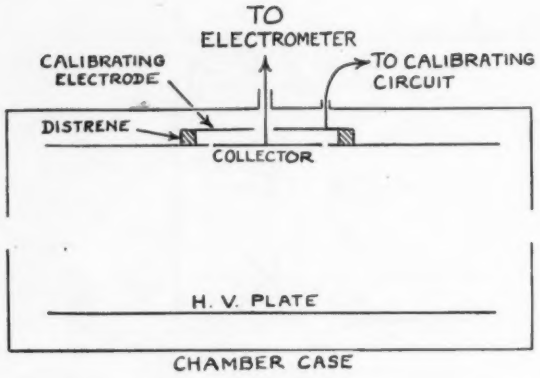

FIG. 3*a*. Lay-out of free-air chamber incorporating a special "calibrating electrode" for use with the comparator.

fects the capacity to earth of the collecting system, and therefore the *calibration* of the instrument.) In such circumstances, the calibration readings must be made *with the guard wires and high voltage plate connected to their normal supplies*.

Special calibrating capacities were therefore introduced into the circuit. To begin with, these took the form of insulated plates placed inside the chamber cases in the proximity of the collecting electrodes, roughly as shown in Figure 3*a*. These could then be connected direct to the ends of the volt-dividing box, as shown in the circuit in Figure 3*b*. It is seen from this figure that

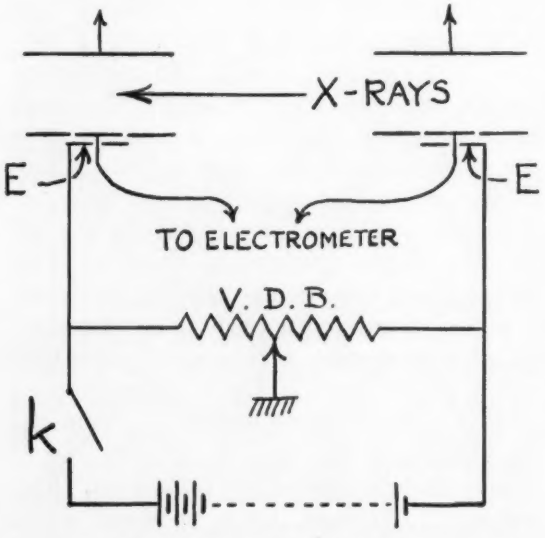

FIG. 3*b*. A much simplified circuit for point-by-point calibration, made possible by the use of "calibrating capacities" (*EE*).

considerable simplification of the calibrating circuit has now become possible, a single tapping key k being the only switching required. Normally, during the collection of the chamber charges under the action of roentgen rays the key k is left open, and no current flows in the volt-dividing box. The calibrating electrodes are therefore at *earth* potential, and behave virtually as parts of the chamber casing. Then, after balancing the comparator, its three earthing keys S_1, S_2 and S (Fig. 1) are closed as usual, and the charges collected are thereby cancelled. Calibrating charges may now be induced on the collecting electrodes simply by closing k, opening S_1, S_2 and S again, and finally reopening k, a procedure exactly equivalent to that described for the earlier circuit.[6] The volt-dividing box setting is then varied until a balance is obtained by this sequence of operations, at the particular setting of C_2 which it is desired to calibrate, the corresponding charge ratio Q_1/Q_2 for balance thus being determined to four figure accuracy from the volt-box reading.

The introduction of calibrating electrodes into the chambers is not always possible, of course, for example where one or more thimble chambers are being used in precision work. In this case alternative procedures are available, as follows: Where a comparator is already in existence, and modifications to the instrument itself are are considered undesirable, two calibrating capacities (identical for convenience) may be employed, a suitable design being shown in Figure 4*a*. They are plugged into the input sockets of the comparator, in place of the chamber cables, the plug fittings at A being identical with the chamber cable plugs. The latter are plugged into the sockets at B, which are identical with the comparator input sockets. Between A and B is a simple cylindrical capacity C, incorporating high insulation at D, the inner electrode being a rod joining the center pins of A and B, the outer electrode being taken to an insulated pin at E. The capacity between the center conductor and the cylinder is of the order of a few $\mu\mu$F. The ends of

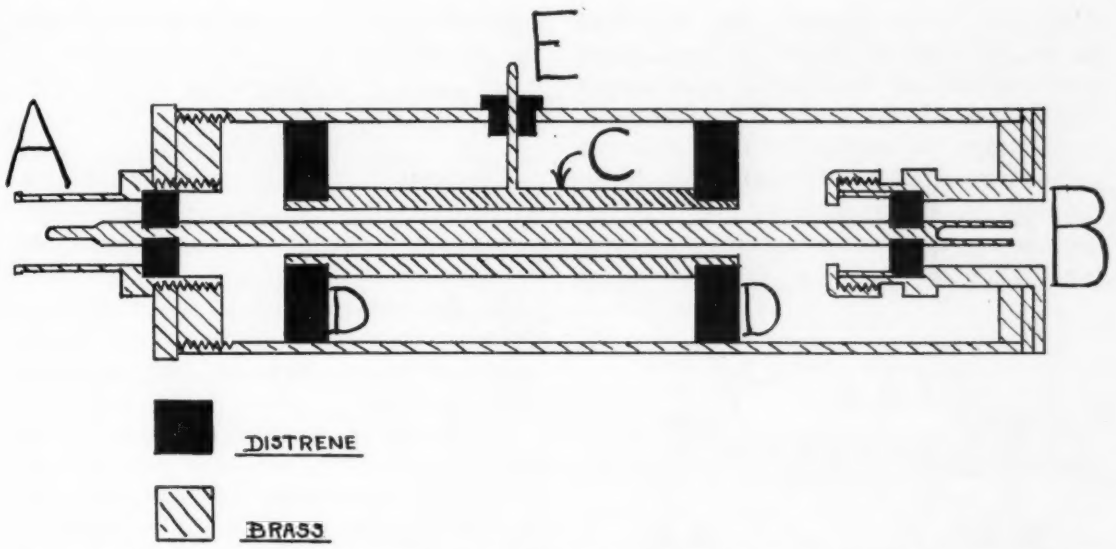

Fig. 4*a*. A "plug-in" calibrating capacity, two of which can be used for point-by-point calibration without structural modification of an existing comparator.

the volt-dividing box are connected to the two terminals *EE* (see Fig. 4*b*), the rest of the circuit, and the experimental procedure when calibrating, being exactly as described for Figures 3*a* and 3*b*. Where a comparator has yet to be built, particularly if it is to be employed in precision work, it is simpler (and neater) to incorporate the calibrating capacities in the instrument itself; for example, they may take the form of cylindrical sleeves mounted around the vertical rods which carry the chamber earthing contacts at the top (Fig. 5). A further possibility is that of building-in the volt-dividing box itself, together with the calibrating key, thus making the whole instrument self-contained. Such an arrangement would be particularly suited to a permanent free-air chamber installation for the calibration of thimble chambers, a brief description of which is given below.

One other addition to the comparator is worth noting here. In such work (*i.e.*, the study of thimble chamber characteristics) it may be necessary to obtain an absolute measure of an ionization current, and for this purpose a Townsend balance circuit is the most suitable. The comparator electrometer system can be employed for this, provided that an input socket, identical with the normal chamber input sockets, is fitted as a means of obtaining a direct connection with the electrometer grid. The chamber whose ionization current is to be

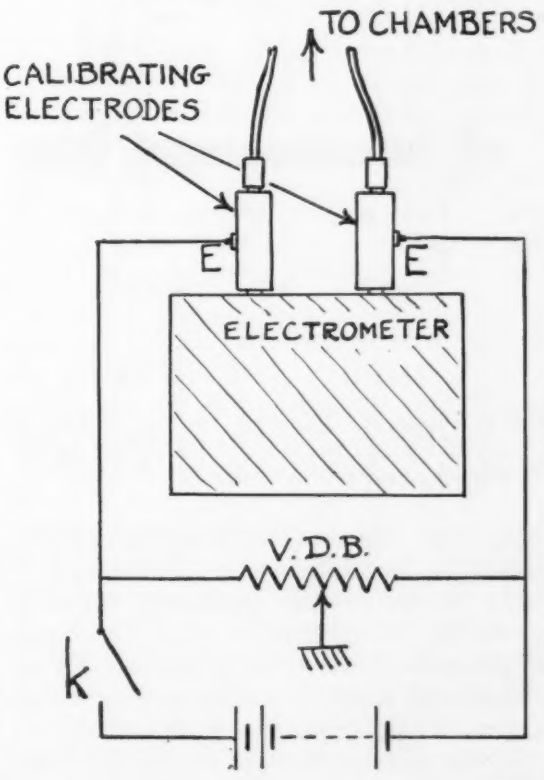

Fig. 4*b*. Diagrammatic indication of the lay-out of comparator and calibration circuit when plug-in calibrating capacities are employed.

measured is then plugged into this third socket, the fixed component of the capacity potential divider then being available as the Townsend condenser. The compensating voltage is applied to the chamber socket connected to this component of the capacity potential divider, and must be *variable* by means of a suitable calibrated potentiometer (such as a volt-dividing box, Fig. 6). The variable component should be set to its lowest value to reduce to a minimum the grid-earth capacity of the electrometer valve, while the input of the socket associated with it should be closed with a simple screening plug which also earths the center pin of the socket.

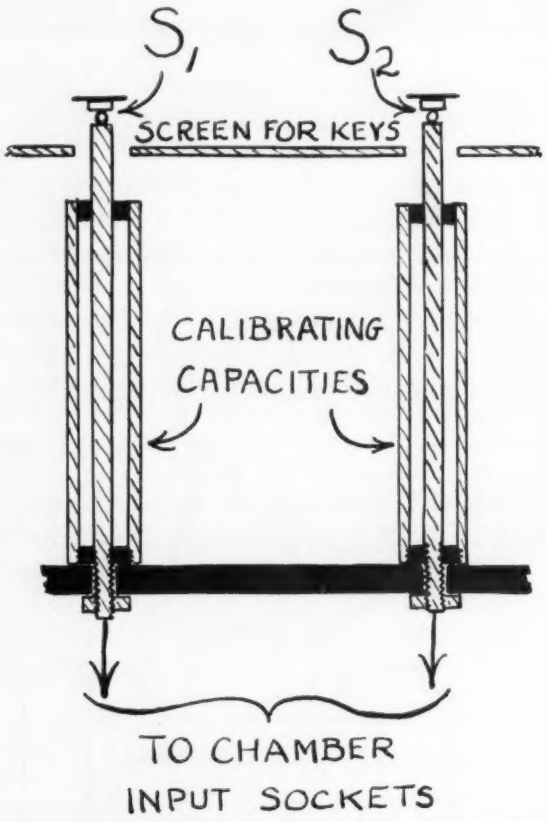

FIG. 5. A suggested design for "built-in" calibrating capacities suited to the well tried lay-out for the chamber earthing keys S_1 and S_2.

To summarize, then, it is seen that with the simple additions discussed in this section, very high precision, coupled with considerable versatility, can be achieved with the comparator.

RECENT APPLICATIONS AND FUTURE POSSIBILITIES

The coaxial free-air chamber pair referred to briefly at the beginning of the last section has been employed in a wide variety of experiments.

(a) By varying the distance between chamber centers, air absorption measurements could be made by the "chamber shift" method.

(b) By placing a suitable tube with very thin (perspex) end-windows between the chambers, absorption measurements on any gas (including air) could be made by filling the tube with gas and varying the pressure.

(c) By providing the second chamber with a pressure casing, and varying the air pressure inside it, studies of the effective plate spacing necessary at different kilovoltages were possible. (Relative ionization in different gases might also be studied.)

It is hoped in the near future to report in detail on many of these measurements.

In the meantime, some reference must be made to what is felt to be an important new

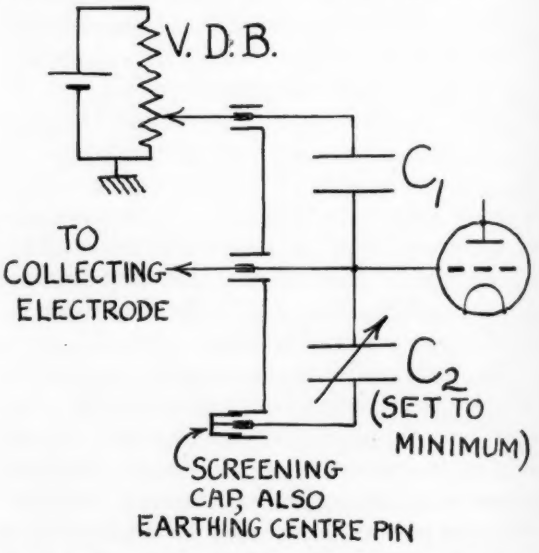

FIG. 6. Suggested circuit and plug-and-socket arrangement for Townsend balance measurements using the comparator.

experimental technique, at present being studied. This is illustrated diagrammatically in Figure 7. A thimble chamber (*B*) is irradiated by a narrow pencil of roentgen rays passing through the free-air chamber (*A*). The two chambers are coupled to the comparator, and the ratio of the thimble chamber response to that of the free-air chamber can thus be obtained over any desired quality range, simply by changing the filtration or kilovoltage (or both) of the roentgen-ray set, and balancing the comparator for each of the qualities selected. Each comparison will take a matter of seconds only to perform, and the results can be plotted at once as a curve giving the variation in the thimble chamber response *relative* to that of a free-air chamber.* This will enable thimble chamber design (from the quality dependence point of view) to be studied with great ease and rapidity. Moreover, to convert quality dependence curves obtained in this way into *absolute* calibration curves for the thimble chamber, all that is required is a single comparison between the free-air chamber and the thimble chamber at one point on the curve in terms of actual roentgens observed, using the Townsend balance arrangements suggested above. Such a procedure should greatly facilitate the standardization of cable-connected dosimeter chambers, and in view of the fact that a special cable connector can always be employed even for Victoreen-type chambers,† the technique would be available for this important class of chamber also. Finally, in this connection it may be noted that it appears possible to adapt the auto-dose plotter circuits[5] for the automatic plotting of thimble chamber quality dependence curves, the "exploring" motor being attached to the variable capacity of the comparator, and the "traversing" motor to a continuously variable filter in the roentgen-ray beam.‡ This development, however, belongs definitely to the future!

* With advantage, the free-air chamber could have a subdivided collector plate system, making it possible to vary the air column length from which ions are drawn, and thus enabling one to obtain comparable ionization currents from the free-air and the thimble chamber, whatever the size of the latter.

† I am indebted to my colleague, Mr. M. Cohen, B.Sc., A.R.C.S., A. Inst. P., for making this point.

Greening's Modification for the Achievement of a Linear Calibration

The techniques and procedures described above have all had the aim of achieving the highest possible precision, as for example, in chamber standardization work; and, clearly, where point-by-point calibration of the instrument is adopted as part of the necessary experimental procedure, non-linearity of the calibration curve is of little consequence.

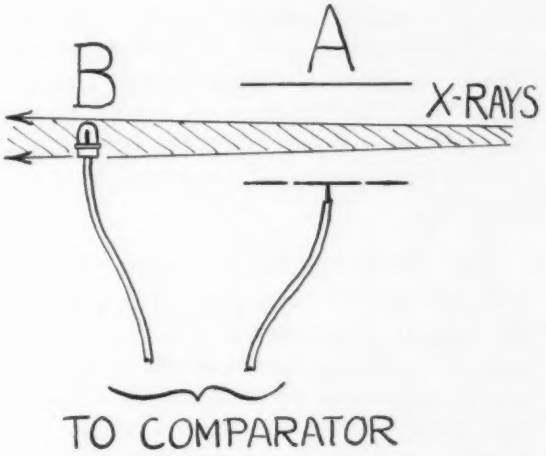

Fig. 7. Arrangement of free-air chamber, *A*, and thimble chamber, *B*, for rapid measurements of thimble chamber quality dependence, using the comparator.

For routine clinical measurements, however (such as those of half-value layer, percentage depth dose, cross-field distributions etc.), it is a great advantage to have a direct-reading, and preferably *linear* dial attached to the instrument, and Greening[1] has described how this may be achieved by the addition of a second variable condenser to the electrometer system, ganged to C_2 (Fig. 1). The arrangement has the further advantage of making the calibration virtually independent of the chamber

‡ *Absorption* curves also, presumably, could be plotted automatically in a similar manner.

cable capacity, thus enabling different chambers to be plugged in without affecting the direct-reading qualities of the arrangement.

A further suggestion made by Greening is that of making the (normally) *fixed* component of the capacity potential divider adjustable in value, so that in making observations which are to be expressed as percentages of a standard reading, the latter may be made to correspond to "100" on the direct-reading scale by pre-setting the "fixed" capacity potential divider component. The other readings in the series are then obtained direct from the instrument dial, as percentages of the standard reading.

THE CHOICE OF THE NULL-INDICATOR

It has already been pointed out that a Lindemann electrometer may be used in place of the electrometer triode as the balance detector, and we shall conclude this review with a brief comparison of the advantages and disadvantages of these alternatives.

(a) Where the highest sensitivity is to be attained, the electrometer valve is required. To achieve this highest sensitivity, coupled with adequate stability and freedom from drift, it is necessary, however, to use accumulators to supply the electrometer voltages, to allow a warming-up period of the order of half an hour, and to take care to adjust the valve bias so that it corresponds to "floating grid potential" conditions. On the other hand, for routine work to an accuracy of, say, 1 per cent or so, the warming-up period can be very much shortened, bias conditions are less critical, and there seems no reason why dry batteries, of reasonable capacity, should not be employed as voltage supplies, at any rate to provide the anode and bias potentials.

In comparison, the Lindemann electrometer is sensitive enough for all but work of the highest possible precision, it needs no warming-up period, and there is no possibility of drift with it.*

(b) The initial cost of a Lindemann electrometer is considerably higher than the corresponding electrometer valve system.

(c) Observations are not quite so easily made with a Lindemann as with the electrometer valve system (microscope eye piece scale readings as against galvanometer readings) unless a projection system is employed.

(d) Where automatic measurements are contemplated[5] (see also references above, to other possible automatic procedures) a mirror galvanometer (and therefore a valve electrometer system) is essential as a balance indicator. There seems no reason, however, why the balance indicator should not be a detachable unit, so that a Lindemann unit could be used for portability, and a valve electrometer unit for other applications to which it was better suited.

SUMMARY

A fuller theory has been developed of a simple ionization current comparator (described in earlier papers[2,3,4,5] and a comparison between a calibration based on this theory, and one carried out experimentally by a precision method (also described earlier[6]) shows agreement to almost one part in a thousand, a demonstration of the high precision attainable with this instrument. This precision has been exploited in the most recent applications (to free-air chamber work) to which reference is made. An indication of the many routine applications, and a brief discussion of alternative design features, based on the most recent experience with the instrument, are also included. Some reference is also made to a number of developments envisaged for the future.

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* Freedom from the possibility of drift in the electrometer itself may be an important factor enabling drifts due to external agents (*e.g.*, stray radiation reaching the electrometer system) to be detected with certainty.

REFERENCES

1. Greening, J. R. Modification of Kemp ionization current comparator. *Brit. J. Radiol.*, 1953, *26*, 53–54.
2. Kemp, L. A. W. New circuit with special applications in gamma-ray and x-ray dosimetry. *Brit. J. Radiol.*, 1945, *18*, 107–112.
3. Kemp, L. A. W. Direct-reading x-ray intensity comparator, radiological and physical applications. *Brit. J. Radiol.*, 1946, *19*, 233–242.
4. Kemp, L. A. W. Physicist in radiodiagnostic department. *Brit. J. Radiol.*, 1946, *19*, 304–313.
5. Kemp, L. A. W. Exploration of x-ray dose distribution; automatic method. *Brit. J. Radiol.*, 1946, *19*, 488–501.
6. Kemp, L. A. W. Method of calibrating ionization current comparator without reference to radiation. *Brit. J. Radiol.*, 1951, *24*, 211–213.

THE PRINCIPLES OF DILATANCY APPLIED TO TECHNIQUES OF RADIOTHERAPY*

By WARREN J. MEAD, PH.D.,† and VINCENT P. COLLINS, M.D.‡

DILATANCY. The property of granular masses of expanding in bulk with change of shape. It is due to the increase of space between the individually rigid particles. Century Dictionary.

This property of granular aggregates was described by Osborn Reynolds,[2] whose interest was apparently confined to its application in his mechanistic concept of the nature of the ether. Little attention has been given to the application of dilatancy and it has important bearing on many geological situations.[1]

A granular mass expands in bulk with change in shape. If expansion is restricted, the mass resists deformation and, if prevented, the mass acts as a strong solid. A rubber balloon filled with rigid-grained material is soft and pliable. If through a suitable arrangement of perforated stopper and pressure tubing, air is pumped from the container, the mass first becomes moldably plastic and with continued evacuation, rigid. This is due to the restraining effect of atmospheric pressure brought into play by reduction of pressure within the bag, thus preventing dilation, and to the increase in intergranular friction as the grains are pressed closely together. High vacuum is not required to produce satisfactory rigidity. An ordinary laboratory aspirator on the water tap is adequate.

The compressive or sheer strength of the evacuated mass is considerable. The tensile strength is low; per unit area it cannot exceed atmospheric pressure. Consequently, flat or long bags have little resistance to cross-bending.

One of the authors (W.J.M.), a geologist, has long believed that there are many situations in which this principle could be used advantageously, particularly in those fields of medical and surgical practice requiring a clean, rapid method of making molds or impressions and in the comfortable support or fixation of all parts of a patient's body. At the suggestion of J. Edward Spike, Jr.,* who had firsthand knowledge of these ideas, the applications of the principles of dilatancy to the techniques of radiotherapy have been explored.

The principles of dilatancy have proved useful in radiotherapeutic techniques in three ways:

1. Fixation of the patient under treatment.

2. A bolus material to build irregular parts to uniform volumes so that dosage distribution can be more readily calculated and controlled.

3. The taking of rapid impressions for the construction of molds and casts.

The basic items required are an elastic, thin-walled container such as a rubber or plastic balloon, containing a quantity of fine granules of close to unit density, and a vacuum pump. The bag is sealed with a one-holed rubber stopper fitted with a short piece of metal tubing. Internally, this is attached to a length of perforated rubber or plastic tubing covering with a fine bolting cloth filter (Fig. 1). Externally, the metal tube is connected with a vacuum pump with plastic or rubber pressure-tubing. It is essential that the balloon and all connections be air tight. Water instead of air may be used as the fluid medium in the balloon. This has the advantage, if plastic granules

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‡ Professor of Radiology, Baylor University College of Medicine, Houston, Texas.
This work was aided by an institutional grant from the American Cancer Society, Inc.

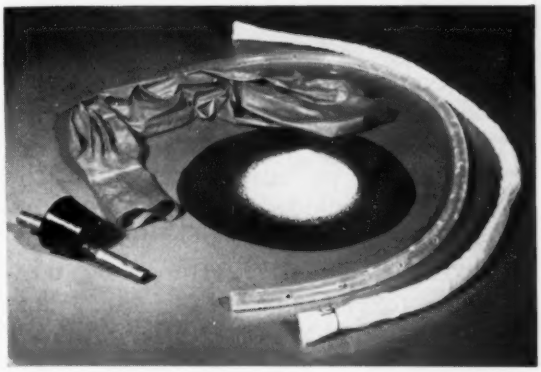

Fig. 1. Disassembled parts—bag and contents, perforated filter tube, sheath, and rubber stopper.

near unit density are used, of bringing the mass within the balloon to unit density desirable in bolus material. When a vacuum is applied to this system, the mass promptly solidifies or "freezes" (Fig. 2). If the system is air tight, the rigidity is maintained indefinitely when the external tubing is clamped.

When used as a method of fixation, the patient or the part of the patient to be treated is placed on a bag of appropriate size and adjusted to the desired position. The flaccid mass (partially evacuated) is manually molded about the part. Full vacuum is then applied and the patient is firmly supported in position by the solidified mass (Fig. 3 and 4). The pressure of the bag on the part to which it is molded is uniform and is neither increased nor diminished by solidification. There is no shrinkage to permit movement of the part and the patient is quite unaware of the solidification of the bag until movement is attempted.

Fig. 2. Assembled unit made rigid by applying vacuum.

Fig. 3. Fixation for a head portal.

Fig. 4. Fixation for a thoracic or abdominal portal.

Fig. 5. Bolus.

Used as bolus material, a thin-walled bag is readily molded to the irregular part to be treated, as in the supraclavicular region or in the axilla. The bag is first evacuated and then a small amount of air is permitted to re-enter so that a malleable consistency is obtained. In this state, the surface may be smoothed as desired either by hand or by a firm flat surface such as the face of a treatment cone. The bag is then solidified by by applying the vacuum and treatment is carried out as if one were using either conventional bolus bags or a wax mold (Fig. 5).

The functions of fixation and bolus may be usefully combined in some sites.

It is common practice to take impressions in plaster of Paris or moulage which requires time-consuming preparation and a period for drying or setting. An impression of the face taken in plaster or moulage may be trying for a patient, particularly if the nose must be included. A negative impression of any part may be taken in a matter of seconds by gently settling the thin-walled sac over the part and solidifying it in position. The bag is then lifted off and a plaster cast of the impression poured. When the plaster has set, separation is obtained by releasing the vacuum. The cast obtained will not ordinarily duplicate fine details but it will accurately reproduce the dimensions and bony prominences usually required for masks, lead shields or radium molds.

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We wish to acknowledge the cooperation of the Dewey and Almy Chemical Company in the development of materials, and the photography of Alfred Puhn in Figures 2–5.

REFERENCES

1. Mead, Warren J. The geologic role of dilatancy. *J. Geology*, 1925, *33*, No. 7.
2. Reynolds, Osborn. Scientific Papers, 1901, *2*, 217.

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A RAPID METHOD OF POSITIONING FOR ROTATION THERAPY

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THE favorable dose distributions obtainable with rotation therapy makes it the treatment of choice for many problems previously handled by single or multiple field techniques. One disadvantage of rotation therapy is the long time required to position the patient correctly. The method described in this paper, which has been used at this hospital for the past two years, removes these difficulties and enables one individual to set up a patient in less than three minutes.

The technique of rotation therapy requires that the patient be rotated about a vertical axis passing through the tumor. A horizontal roentgen-ray beam is then directed at this axis.

One sequence of steps by which a patient can be positioned for the above treatment is shown in Figure 1. The horizontal roentgen-ray beam is first adjusted so that it passes over the center of the circular rotating platform, through an imaginary vertical axis (Fig. 1*A*). The problem now is to move the patient over the platform so that his tumor coincides with this axis. A common way to do this is to mount the vertical column, seat and supporting crossbars on a set of traverses which permit motion in two perpendicular directions. Figure 1*B* shows the cross section of a patient who has been securely fastened to the seat and crossbars. The position of his tumor can be described by a distance *d* from a point on the skin along any given horizontal axis, for example, the anteroposterior axis. The patient can then be positioned correctly in the following three steps:

(a) The axis along which the skin tumor distance *d* has been measured is placed parallel to the roentgen-ray beam by turning the platform (Fig. 1*C*).

(b) The reference point on the skin is lined up with the center of the roentgen-ray beam (Fig. 1*D*).

(c) The patient is moved along the beam so that the reference point on his skin is a distance *d* in front of the center of rotation (Fig. 1*E*).

Most rotating chairs are so constructed that the patient is fastened to the crossbars so that his anteroposterior and lateral axes are parallel to the direction of motion of the two traverses. Therefore the skin-tumor distance is conveniently measured

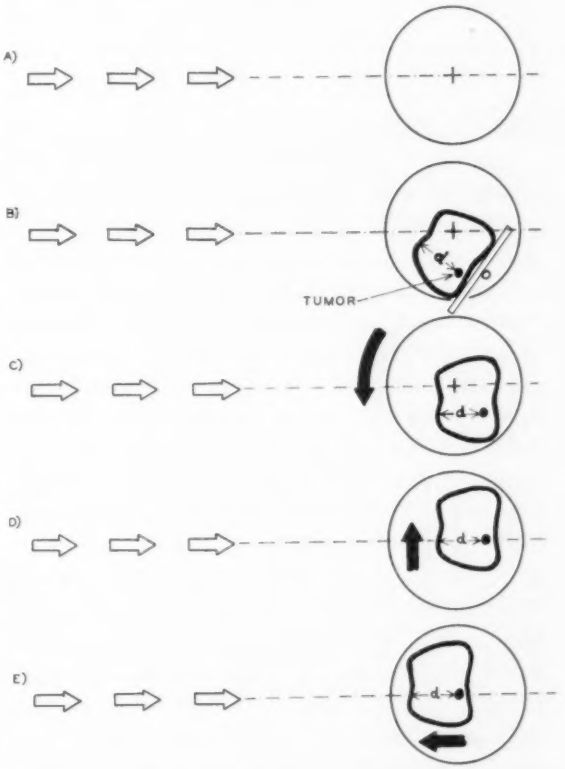

FIG. 1. Steps in positioning a patient: (*A*) roentgen-ray beam lined up with center of rotation; (*B*) patient strapped on chair; (*C*) platform turned to zero position; (*D*) tumor moved into axis of roentgen-ray beam; (*E*) tumor moved to center of rotation.

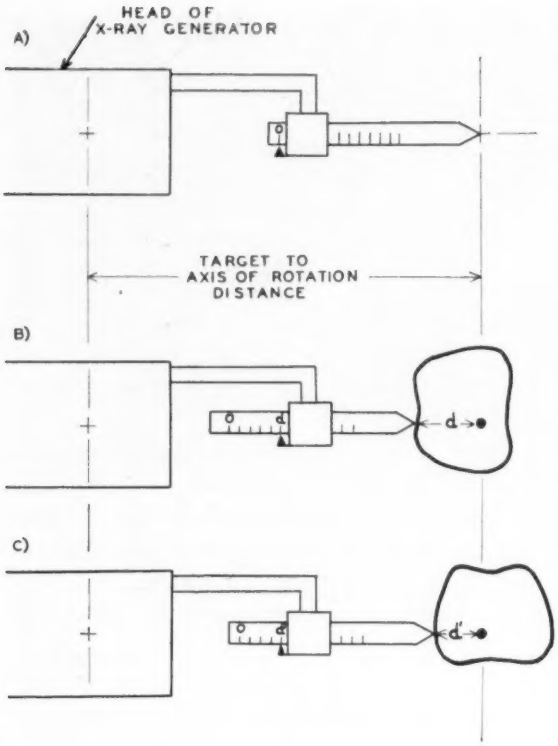

FIG. 2. Use of rotation pointer for rapid positioning.

along the anteroposterior or lateral axis of the patient. In such a case, adjustment (*a*) is the same for every patient. The traverses are now respectively parallel and perpendicular to the roentgen-ray beam. This is called the zero position of the platform. Adjustments (*b*) and (*c*) above are easily made with the aid of a pointer of special design mounted on the roentgen-ray machine as shown in Figure 2. The graduated rod lies in the central axis of the roentgen-ray beam and can be moved along it. When the pointer is at its zero position, its tip touches the axis of rotation of the platform (Fig. 2*A*). The graduated rod is pulled back a distance *d* (the skin-tumor distance), and the patient is moved on the traverses until the reference mark on the skin touches the tip of the pointer (Fig. 2*B*). The tumor is now in the center of rotation and the patient is ready for treatment.

The accuracy of this procedure can be easily checked by measuring the skin-tumor distance along a second axis, for example, *d'* (Fig. 2*C*). When one rotates the patient so that this second axis is parallel to the roentgen-ray beam, the pointer should read *d'* when its point touches the skin. In practice, this checking procedure has been found unnecessary after the first treatment.

To sum up, one positions the patient in the following four steps: (1) strap the patient in the chair; (2) turn the platform to the zero position; (3) set the pointer to read *d*, the skin-tumor distance; (4) move the patient over the traverses until the reference mark on the skin touches the tip of the pointer.

This can usually be done in about three minutes by one person.

A photograph of the rotation pointer mounted on a General Electric 2 mev. generator is shown in Figure 3.

In order to confirm the accuracy of this method, tests were carried out on a chest phantom. A small lead slug (about 1 cm. in diameter) was imbedded in the phantom and rotation fields of various widths centered on it by the method described. The position of the slug in the field was then checked by taking roentgenograms with the therapy beam for various angulations of the rotating platform.

It is apparent that this method of positioning cannot be more accurate than the determination of the skin-tumor distance *d*. In a phantom, *d* can be accurately measured but it is not so easy to do this in a patient. In a few areas, such as the mouth, *d* can be directly measured on the patient. For lesions located elsewhere, one must depend on measurements based on roentgen films or roentgenoscopy after making necessary corrections for distortion. All roentgenographic and roentgenoscopic examinations should be carried out with the patient in the same position which will be used during treatment. In those cases where, even with the above precautions, *d* cannot be determined accurately (*e.g.*, abdominal lesions in obese persons), additional information should be obtained from

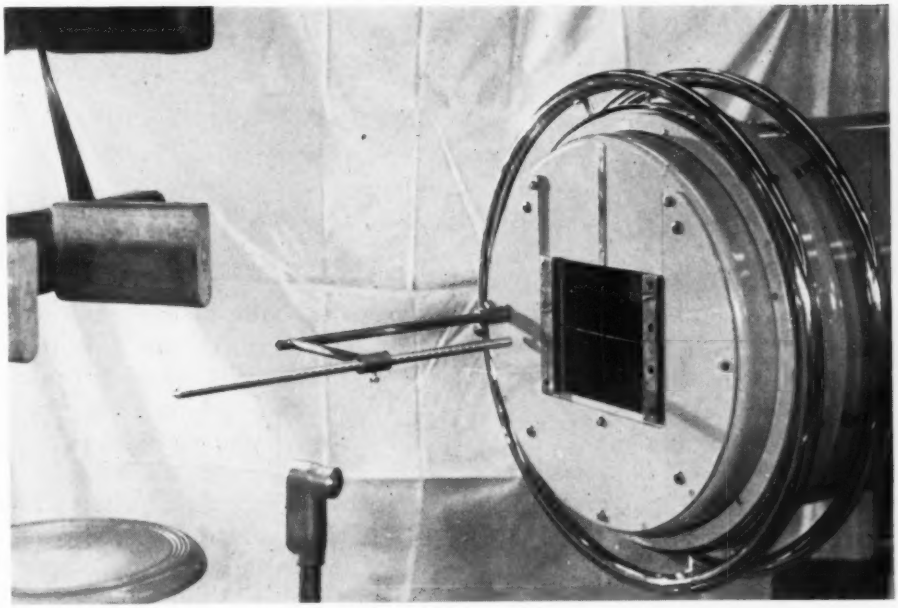

Fig. 3. Rotation pointer mounted on General Electric 2 mev. generator.

roentgenograms taken with the therapy beam at the time of the first treatment. It is important that the patient be strapped on the platform in such a manner that the skin-tumor distance remains constant during all subsequent treatments.

The over-all accuracy of this method, when *d* can be accurately measured, was verified by taking roentgenograms with the 2 mev. beam after the patient had been positioned. Additional verification of this accuracy was obtained in cases where mucosal reactions in the mouth were found to correspond to the calculated limits of the field after a course of treatments.

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INTRATHORACIC PRESSURE AND POSITION OF THE PATIENT IN THE ROENTGEN EXAMINATION OF THE MEDIASTINUM

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VOLUNTARY changes of intrathoracic pressure have been utilized for diagnostic purposes by Westermark[1] and by many others. During a Valsalva test, the high intrathoracic pressure decreases the amount of blood in the pulmonary vessels. This allows the differentiation of lung conditions where vascular elements produce a large part of the roentgen shadows from other lung conditions where the shadows are due to solid tissue.

Voluntary changes of intrathoracic pressure also cause changes in the roentgen appearance of the mediastinum. The effects of pressure may be enhanced by utilizing the shifting of blood which occurs during sudden changes in the position of the patients. This may be accomplished by combining the Muller test (inspiration with closed glottis) with extreme Trendelenburg position and observating the change in size and shape of the mediastinum which occurs when the patient assumes the erect posture and performs a Valsalva test (forced expiration against a closed glottis). The negative pressure developed during the Muller test, combined with the effect of gravity of the Trendelenburg position causes marked distention of the mediastinal veins. On the other hand, the positive pressure developed during the Valsalva test combined with the gravitation of blood

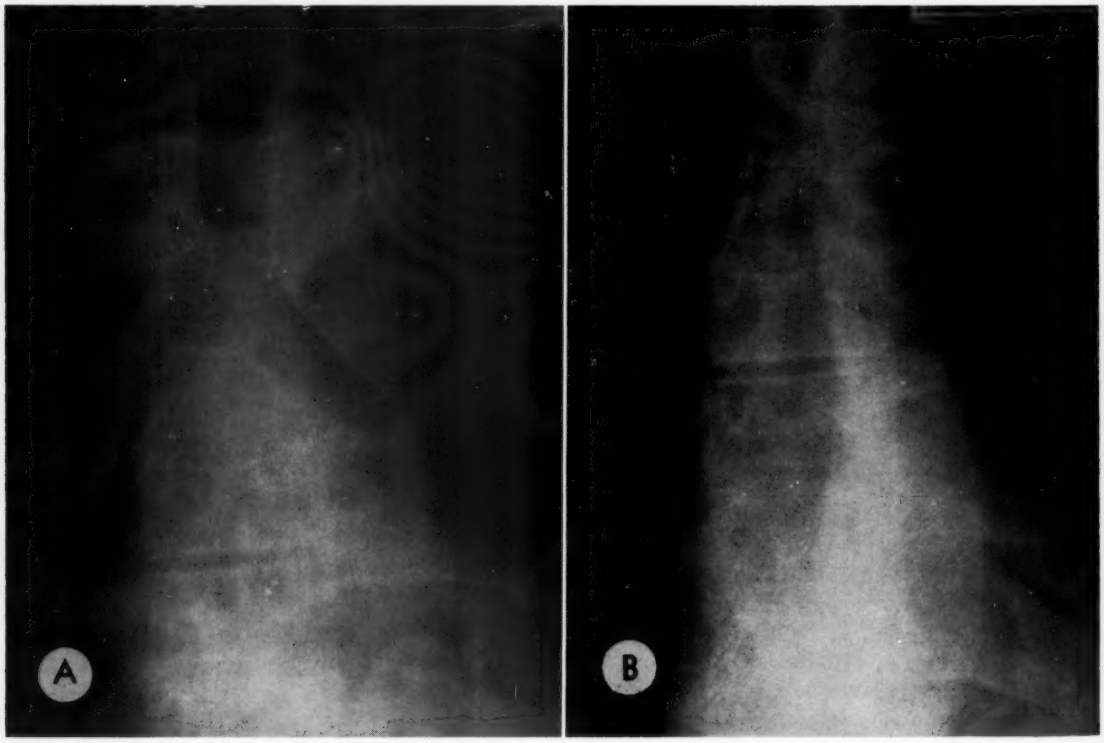

FIG. 1. (*A*) Normal mediastinum during a Muller-Trendelenburg test. (*B*) Same mediastinum during a Valsalva-upright test.

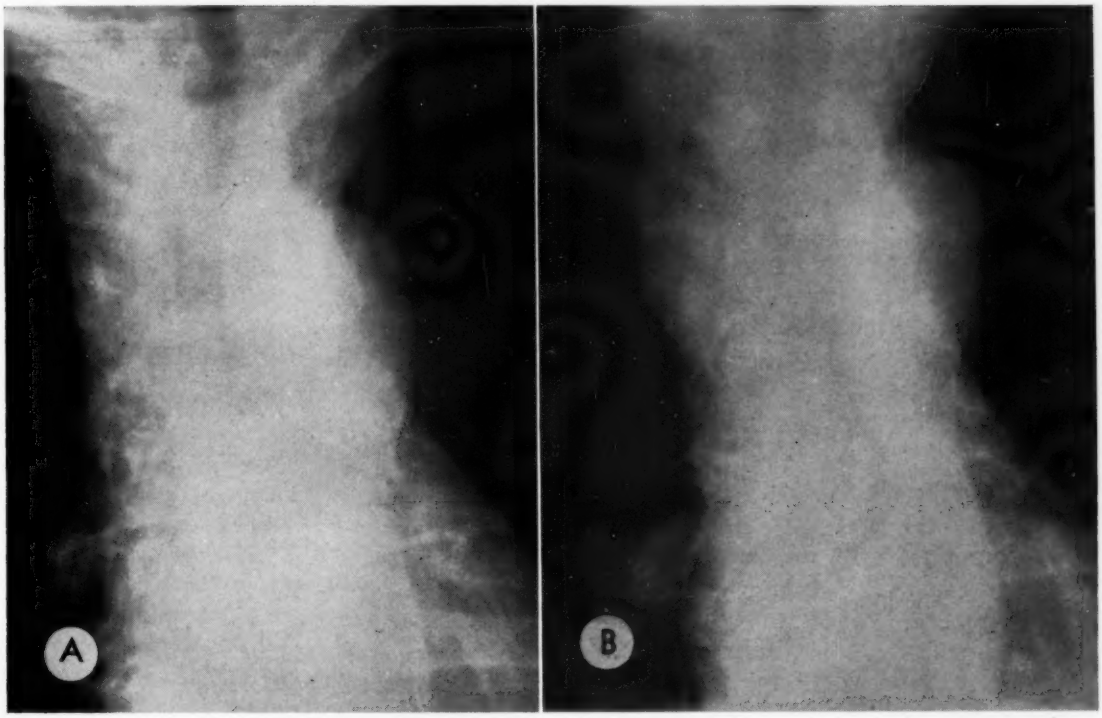

Fig. 2. (*A*) Muller-Trendelenburg test in a case of paratracheal metastasis from carcinoma of the right lung. (*B*) Valsalva-upright study; note the polycyclic contour of the right edge of the upper mediastinum.

toward the lower extremities in the upright position interferes with the venous return and empties the mediastinal veins. The Valsalva test should be prolonged to the point of slight dizziness, but not to the point of causing fainting of the patient. A tilting table with a spot film device is helpful in such a study.

Most of the changes observed during this procedure are due to variation in the distention of the caval system of veins, but the different amounts of blood returned to the heart also cause the size of the heart, of the pulmonary vessels and of the aorta to change in varying degrees. These structures change in size more readily in young persons than in older patients.

In normal individuals, the Muller-Trendelenburg study (Fig. 1*A*) causes maximal distention of the mediastinal veins and furnishes excellent contrast for the visualization of the trachea and of the main bronchi. On the other hand, in the Valsalva-erect posture films, the size of the mediastinal veins is reduced so much that for practical purposes the roentgen appearance of the mediastinum is due only to the arterial components (Fig. 1*B*). This permits a study of the arterial structures at a time when these structures are free from the overlapping shadows of the large veins.

Figure 2 shows a wide upper mediastinum in a patient with carcinoma of the right lower lung. It must be noted that in this patient the width of the mediastinum changes little with changes of position and pressure. During the Valsalva upright test, however (Fig. 2*B*), the emptying of the mediastinal veins discloses a polycyclic contour along the right upper edge of the mediastinum. These findings suggested that the mediastinal widening was due to solid tissue and probably represented metastatic growth in the right paratracheal glands. At surgery, these glands were found enlarged and invaded by carcinoma.

The detection of paratracheal adenopathy probably represents the main indica-

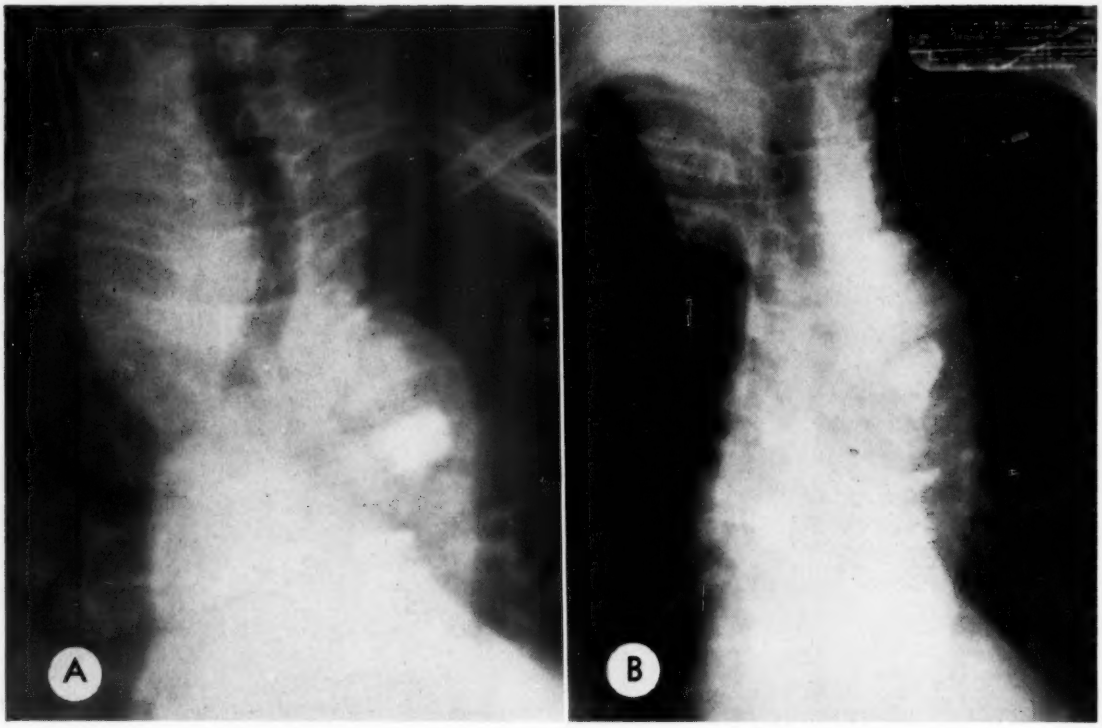

FIG. 3. (*A*) A "goitre plongeant" during Muller-Trendelenburg test. (*B*) Goiter pushed almost outside of the chest during the Valsalva-upright test

tion for pressure-position studies.

Masses located at the entrance of the chest may be markedly displaced by changes of intrathoracic pressure. Figure 3 illustrates the behavior of an intrathoracic goiter (goitre plongeant) which was pushed almost entirely into the neck during the Valsalva-upright test (Fig. 3*B*).

The diameter of a dilated and calcified aorta will change very little with changes in pressure or position because of the rigidity of the walls. For the same reason, one cannot expect much change in the size of aortic aneurysms. The emptying of the venous channels, however, may facilitate the localization of such mediastinal masses and help in establishing their relationship with the aorta.

In the presence of pericardial effusion, variation of intrathoracic pressure will not change the size of the cardiac shadow appreciably. On the other hand, the shape of the cardiac shadow may be altered significantly by changes of position because of the gravitational shifts of the pericardial fluid.

CONCLUSION

Pressure-position studies are of supplementary value in the roentgen diagnosis of mediastinal diseases. Occasionally the observation of the effects of pressure and position permits diagnostic conclusions which would be difficult to obtain otherwise.

REFERENCE

1. WESTERMARK, NILS. Roentgen Studies of the Lungs and Heart. Minnesota Press, 1948.

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NEW EXPLOSION-PROOF AND SHOCK-PROOF MOBILE ROENTGENOGRAPHIC EQUIPMENT FOR THE OPERATING ROOM*

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THE need for improved operating room roentgenographic equipment and technique has been outstanding. In most hospitals, mobile bedside equipment is used in the operating room, with mediocre or poor results, because of the inherent limitations of the apparatus. A solution to this problem is the installation of modern high capacity roentgenographic equipment in the operating room, which is similar or identical to apparatus used for roentgenography in the roentgen-ray department. Obvious disadvantages are the impossibility of making it explosion-proof, high cost of installation, limitation of its use to one room, and decreased space for surgery.

These disadvantages have been obviated by special mobile shock-proof equipment that eliminates the danger of an anesthetic explosion, because only the oil-immersed rotating anode tube, its cables and tube-stand and a full length table-top cassette tunnel are in the operating room† (Fig. 1). The transformer, a potential source of explosion, is mobile and wheeled from its storage place to a station in the corridor just outside and beyond the door of the operating room, prior to the examination (Fig. 2).

The mobile transformer is a type used for bedside roentgenography and is commercially available. Its capacity was doubled to 89 kv. (peak) and 120 ma., by the installation of four-valve tube rectification and a 220 volt line. A synchronous motor-driven timer was added to insure proper timing.

The tube stand supporting a rotating anode tube is also mobile and is wheeled into the operating room before its use, where ceiling mounted shock-proof cables are attached to the tube (Fig. 1). This part of the equipment is then moved out of the way until needed.

Mobility of the generator and tube stand enables their use in any operating room equipped with through-the-wall cables and adaptors that permit quick insertion into the tube at one end and the transformer at the other. The cables extend through the operating room wall at ceiling level to an optimal area near the center of the room. The cables ends are detached when the examination is completed and placed in out of the way wall brackets in the operating room and corridor (Fig. 2). All of the operating rooms in the Germantown Hospital

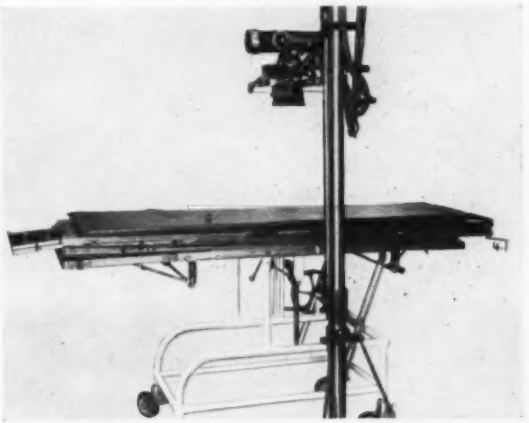

FIG. 1. Mobile tube stand supporting rotating anode tube with attached cables is in position for roentgenography. Grid front cassette in tray is ready to start longitudinal travel beneath table top covered by a plastic radiolucent foam rubber mattress (*1* and *2*). Endless chain carrying cassettes is moved by turning hand crank (*3* and *4*). Table-top tunnel fits on any flat operating room table and is easily stored when not needed.

† The equipment was designed and developed for us by Mr. William Hogan, Franklin X-ray Company, Philadelphia, Pennsylvania.

* From the Department of Radiology, Germantown Hospital, Philadelphia, Pennsylvania. Presented at the Fifty-fourth Annual Meeting, American Roentgen Ray Society, Cincinnati, Ohio, Sept. 29–Oct. 2, 1953.

have been equipped for roentgenography by the installation of cables.

A specially built full length table-top tunnel, with an endless chain for transport of grid-front cassettes eliminates a Potter-Bucky diaphragm and its incorporated electric switch, which is another source of anesthetic explosion (Fig. 1). The table-top tunnel fits on any flat operating room table. It is sturdy and durable, but not excessively heavy, and therefore easily placed in position and stored on end in the small operating floor darkroom, when not in use.

Grid-front cassettes in trays are placed on the endless chain at the foot end of the table and moved by a hand crank until the first cassette is exactly beneath the region of the patient under examination. Movement of the cassette is stopped by a projecting bar attached to a device that slides in the long axis of the table beneath its edge, permitting rapid adjustment of cephalocaudad centering. Following exposure of the first cassette, the stop is momentarily released, and the second cassette is brought into position by forward movement of the endless chain. This action is then repeated after the second exposure is made. By this mechanism, three or four exposures can be made in quick succession or at slower intervals, depending upon the requirements of the examination. Exposed cassettes are removed from the head end of the table, as soon as they emerge.

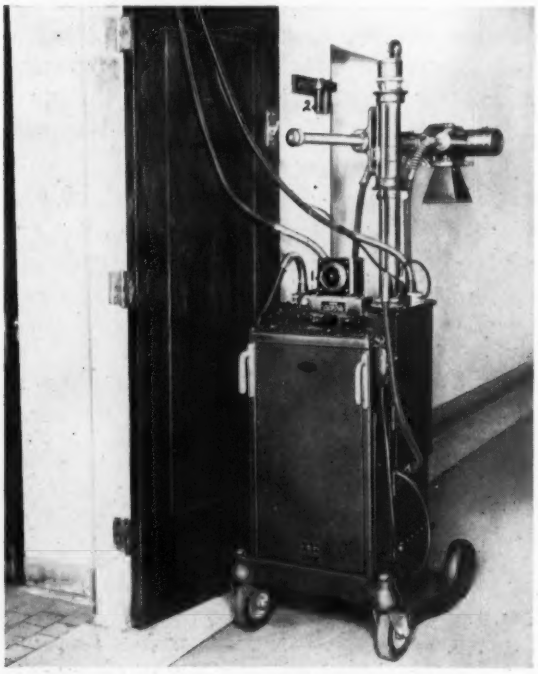

Fig. 2. Mobile transformer stationed in corridor outside operating room has a capacity of 89 kv. (peak) and 120 ma. because of installation of 4-valve tube rectifiers and 220 volt line. Note synchronous motor timer (*1*). Ceiling mounted cables are detached and placed in brackets when examination is finished (*2*). Equipment is also used for bedside examination.

Trays are placed crosswise in the tunnel and fit between its supporting vertical walls, allowing full side-to-side movement, and therefore centering, of the cassette. Thus, any portion of the patient is readily examined, because the cassette can be moved the full length and width of the table. Good quality serial roentgenograms of the abdomen and other parts of the body can be obtained with exposures as short as 1/10 second at a target film distance of 34 inches.

We have used the roentgenographic equipment principally for cholangiography and hip nailing, but much wider utilization is anticipated in the future. Any part of the skeleton is readily demonstrated, and, therefore, examination of the bones, before, during and after surgery can be performed with ease. The method is valuable to determine progress and results of orthopedic and fracture surgery, when roentgenographic guidance is indicated while the patient is still on the operating table. Angiography, venography and a roentgen search for an opaque foreign body or urinary calculus are performed without difficulty with this equipment. This is also true of routine postoperative chest examination to detect atelectasis and other pulmonary complications before the patient leaves the operating table. Thus, effective treatment can be instituted at once with lowering of morbidity.

Operative cholangiography allows the detection of stones in the common duct, common bile duct and biliary radicles and

Fig. 3. Operative cholangiogram obtained immediately after removal of many residual small stones from common and left hepatic duct is negative for calculi. Dilated duct system filled by 20 cc. of 35 per cent diodrast. Common and left hepatic ducts opened after cholecystectomy because initial operative cholangiograms revealed stones (see Fig. 4).

obstruction due to causes other than stone. It is unquestionably indicated when there are clinical findings of obstructive jaundice and also when the operative findings suggest or indicate obstruction of the common duct due to stone or noncalculous disease. Routine cholangiography during cholecystectomy has resulted in detection and removal of unsuspected duct stones. It also has eliminated negative explorations of the common duct and unnecessary T-tube drainage.

Use of a full length table top, tunnel and other roentgenographic equipment, described in the preceding paragraphs, will unquestionably result in increased frequency of operative cholangiography, because delay and interference with surgery are minimized and invaluable visual information about the biliary tract is obtained quickly.

When operative cholangiography is contemplated, the tunnel is placed on the operating table and a cassette positioned beneath the patient before draping. A radiolucent plastic covered foam rubber mattress adds greatly to the comfort of the patient and does not interfere with roentgenography (Fig. 1). A preliminary film is exposed to make certain of proper technique before surgery is started. Adjustments in technique are made, if necessary, and then three cassettes are placed on the endless chain at the foot end of the table, and transported to their positions by turning a hand crank. By spacing the cassettes on the endless chain, 5 inches apart, fogging from scattered radiation is eliminated. When the cassettes are placed next to each other, the film nearest the one under exposure shows fogging, and therefore it must be protected by lead rubber placed above it on the table top.

Successful operative cholangiography is dependent on good roentgenographic equipment and technique, and teamwork of the surgeon, anesthetist and radiologist. The biliary tract must be well filled with an opaque, water soluble solution, breathing must be suspended, and roentgenograms of good technical quality obtained (Fig. 3). Twenty cubic centimeters of 35 per cent diodrast is usually adequate, but as much

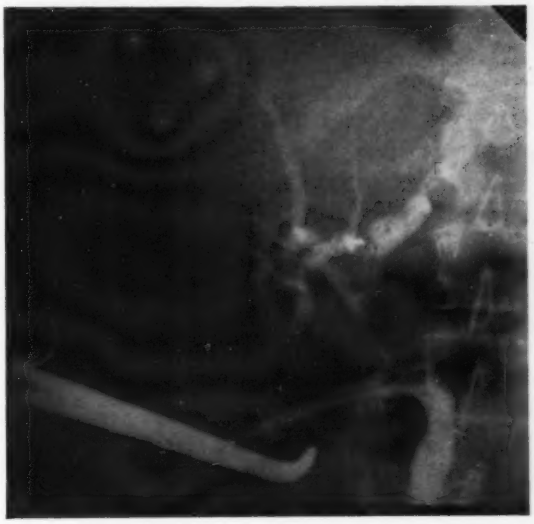

Fig. 4. Calculi in common bile and left hepatic ducts revealed by operative cholangiography. Residual stones demonstrated by postoperative cholangiograms necessitated a second surgical exploration of the duct and removal of remaining calculi (arrow). Third set of cholangiograms negative for stones (see Fig. 3).

as 30 cc. is required when the biliary tract is greatly dilated. Serial films are superior to a single film in the demonstration of obstruction and in the differentiation of nonopaque stones from injected air.

Satisfactory visualization of the biliary system reveals stones or obstructive disease of the common and biliary ducts, and thus indicates whether the common duct need be opened (Fig. 4). After corrective surgery, subsequent operative cholangiography is in order to eliminate a small residual stone that has escaped detection during exploration. Postexploratory operative cholangiography obviates closure in the presence of one or more residual stones (Fig. 4).

The use of this equipment has facilitated roentgenography of the hip during internal fixation of fractures of the upper end of the femur. End loading and removal of films lessens interference with the surgeons and shortens the roentgenographic procedure, because unexposed cassettes are quickly brought into position by movement of the hand crank. Thus, anteroposterior films are obtained with a minimum of effort.

For the lateral view of the hip a special cassette-holding device is used (Fig. 5). An unexposed cassette is held in a tunnel in an out of the way position, lateral to the patient's upper abdomen and lower thorax, and moved into position by rotating it on a vertical upright post, attached to a flat base. The metal base is held in position on the table-top tunnel by the weight of the patient (Fig. 5). After the film is exposed, the vertical cassette tunnel is pivoted to its former position alongside the patient's lower chest.

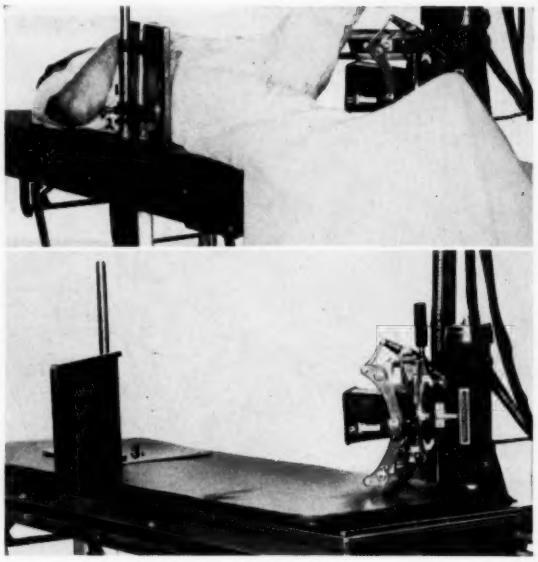

FIG. 5. Cassette holding device for lateral view of hip. Cassette rotates 360 degrees on vertical bar and therefore is readily moved into position for exposure from out-of-the-way resting place alongside the thorax and axilla (*1*). Adjustable collar allows elevation and lowering of cassette (*2*). Flat base is placed beneath thorax and held firmly by weight of patient (*3*). Placement of the patient's arm on a side extension board permits rotation of cassette holder to the lateral thorax for loading and unloading.

SUMMARY

New mobile explosion-proof and shockproof roentgen-ray equipment has been developed that eliminates the danger of an anesthetic explosion and facilitates roentgenography in the operating room. The remote possibility of an explosion because of puncture of the tube end of a cable has been eliminated by sheathing with plastic rubber. Installation of through-the-wall cables at ceiling level allows placement of the transformer outside of the operating room in the corridor and thus obviates a potential source of explosion. A rotating anode tube on a mobile stand is used in the operating room. Since both the transformer and tube stand are mobile, they can be used in any operating room, equipped with cables, or for bedside roentgenography. Placement, removal and storage of this equipment are not difficult and therefore it does not need to take up valuable operating room space when not in use.

An end-loading full length table-top tunnel with an endless chain carries films beneath the patient in longitudinal travel, thus minimizing interference with surgery during serial film examination. Any part of the patient can readily be examined when this tunnel is used. To date, the equipment has been used principally for operative

cholangiography and roentgenography during hip nailing procedures. A specially designed cassette tunnel is used for lateral views of the upper end of the femur during hip nailing.

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DISCUSSION

Dr. Russell H. Morgan, Baltimore, Maryland. There is no question but that the roentgen examinations associated with procedures conducted in the operating room have become sufficiently important to demand the use of the best possible roentgen-ray equipment. Unfortunately, the complexity of the procedures undertaken in surgical practice frequently prevent us from reaching this objective, but it is gratifying to see how well Dr. Young and his colleagues in Philadelphia have been able to reach a satisfactory solution to the problem.

It is too bad that all of us are not as fortunate as the Philadelphia group of radiologists in having at our disposal an organization like Mr. Hogan's that can take care of our special needs as they arise. There are very few cities where such a situation exists. Possibly the Boston area is the only other.

As far as our own hospital is concerned, we are currently preparing to install 300 milliampere apparatus in several of our operating rooms where the radiological activities are particularly heavy, and we have taken care of the situation as far as the explosion-proof requirements are concerned in a manner similar to those adopted by Drs. Young and Scanlan, by keeping the controls and transformers out of the operating area itself and in adjacent anterooms which have been especially designed for that purpose.

There is one thing that Dr. Young did not mention, which we have found very worth while, and that is the inclusion in the operating suite of a first class dark room, in which films can be processed rapidly and under essentially identical conditions to those used in the radiological suites to produce films of the best possible quality.

With the work that Dr. Young is doing, I hope the roentgen-ray manufacturers of this country now may seriously get to work on the problem of producing equipment which we can use effectively in the operating rooms. As Dr. Young so ably pointed out, the need for such equipment is very great indeed.

USE OF POLAROID LAND CAMERA FOR COPYING ROENTGENOGRAMS

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THE copying of roentgenograms is finding increasing application. Chief among these are:

1. It provides the best possible material for reproduction[1] in publishing case reports.

2. Many publishers make reproductions that are facsimile in tone only from paper duplicates. This type of copy should always be submitted with the manuscripts. When roentgenograms are submitted, they are often reproduced with the tone relations reversed. Such duplicates may tend to be confusing to readers; they are therefore not as useful as same-tone duplicates.

3. Inclusion of small-sized copies of roentgenograms adds materially to the clarity of the transcript when the individual moves to another locality.

4. Inclusion of small-sized copy of a roentgenogram with the report to the referring physician, where pathology is demonstrated, is of inestimable value to the physician in evaluating the report.

The previous methods of copying roentgenograms involved the utilization of a process of making an intermediate and then a duplicate of that by either: (1) contact printing, employing a contact printer or a printing frame; (2) projection printing, employing an enlarger; (3) photographing

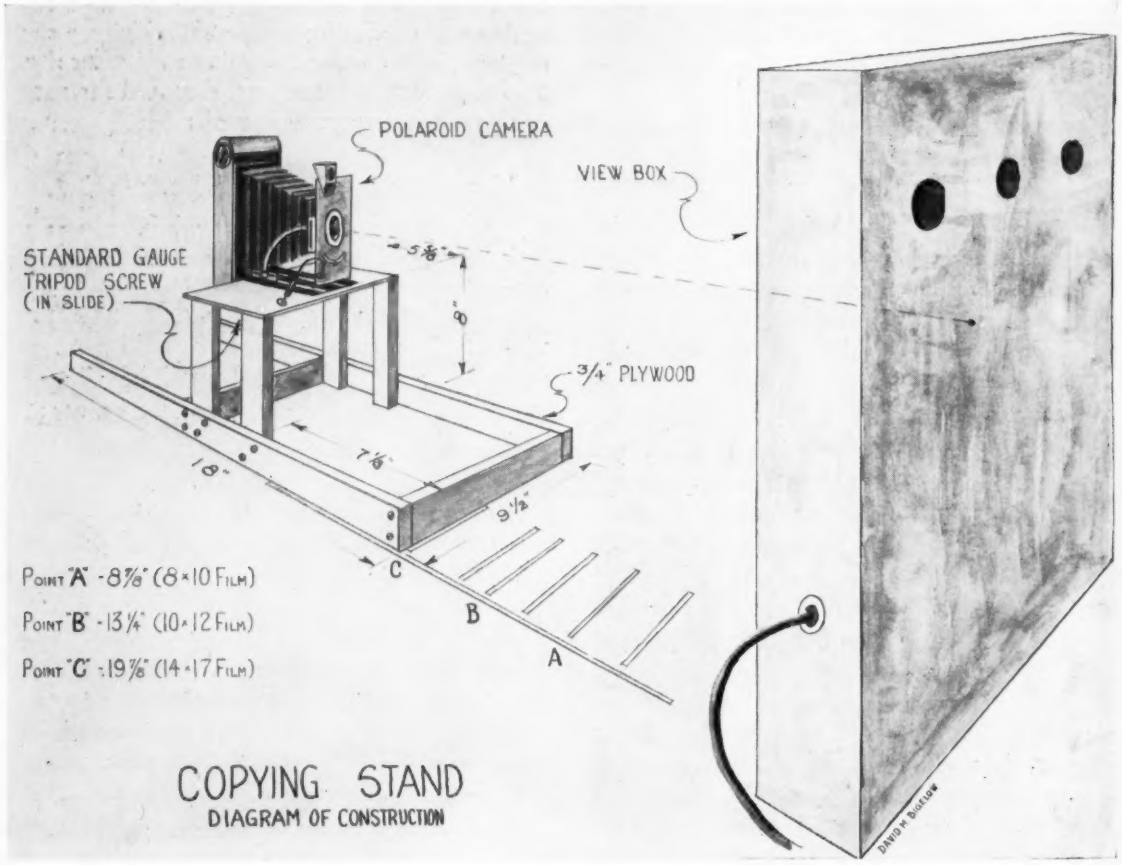

FIG. 1.

Fig. 2. Fracture of the os calcis.

the intermediate on film or plate, by using the camera in the same manner in which it is employed for making the intermediate.

Another recent technique[2] is the copying of roentgenograms with miniature kodachrome film, also employing a basic preexposure technique. The disadvantage of this method is the small size of the film (35 mm.).

The author has found that the use of the polaroid Land camera offers many advantages, such as: (1) omission of the intermediate phase; (2) adequate size of the copy ($3\frac{1}{4}$ by $4\frac{1}{2}$ inches); (3) no necessity for dark room equipment; (4) prompt evaluation of the copy after exposure (one minute). In practice, copies of roentgenograms which list pathology or significant findings are most likely to be useful. These are transmitted with the written report to the referring physician.

A diagram of the copying stand which I employ is shown (Fig. 1). In practice, the stand is placed on any working counter and moved to varying distances from the illuminator, according to the size of the film to be copied. The stand is centered to the illuminator. Thus, the lower front part of the stand would be placed at Point A ($8\frac{7}{8}$ inches away) for an 8 by 10 inch film;

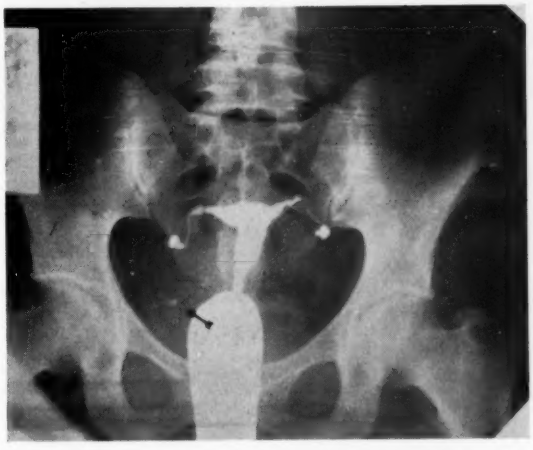

Fig. 3. Uterotubogram illustrating fine detail of uterine tubes.

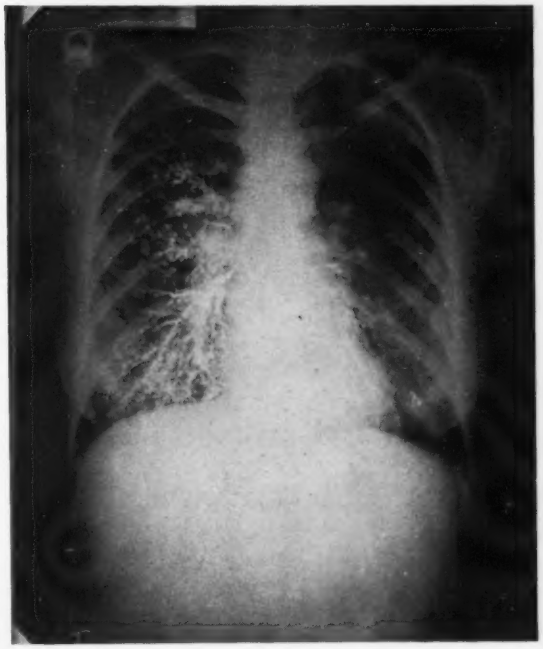

Fig. 4. Bronchogram.

Point B ($13\frac{1}{4}$ inches) for a 10 by 12 inch film; and Point C ($19\frac{7}{8}$ inches) for a 14 by 17 inch film. The 10 by 12 and 8 by 10 inch films are centered in the 14 by 17 inch illuminator, which is elevated $2\frac{1}{4}$ inches above the working stand, either with scotch tape or by the use of masks. A set of portrait lenses is furnished with the polaroid camera.

Depending on the size of the film, Table 1 below lists the number type of portrait lens to be used, as well as the setting for the camera focus. For example, if a 14 by

Fig. 5. Calculi in gallbladder.

17 inch film is to be copied, the camera is placed at Position C, a No. 1 portrait lens is used, and the camera focus is set at 8 feet.

A final word of admonition: If considerable light comes through the roentgen film the exposure setting, regulated by the shutter setting disc of the polaroid camera, is placed at No. 2 (this is a single adjustment which sets both lens and shutter speed); if little light comes through, the exposure setting is placed at No. 1. An instantaneous exposure is made. At setting No. 1, this is equivalent to $f/11$ at $\frac{1}{8}$ second; at setting No. 2, this is equivalent to $f/11$ at $\frac{1}{15}$ second.

Table I

	14″ by 17″ film	10″ by 12″ film	8″ by 10″ film
Portrait lens number employed	+1	+1	+2
Camera focus distance	8′	4′	10′

Samples of positive prints illustrating various types of films are shown (Fig. 2, 3, 4 and 5).

SUMMARY

1. A new method of copying roentgen films, employing the polaroid Land camera, is described.

2. The details of this technique are enumerated.

3. Positive prints illustrating a variety of applications are presented.

219 Walnut St.
Evansville 8, Indiana

Thanks are due to Mr. Donald Hendershot of Smith and Butterfield for his able assistance and cooperation in helping to devise the copying arrangement, and to Mr. David Bigelow of the Evansville Public Museum for the drawing of the stand.

REFERENCES

1. Brownell, C. G. Making copies of radiographs. *Med. Radiog. & Photog.*, 1951, *27*, No. 4, 114–121.

2. Gibson, H. L. Copying radiographs with miniature kodachrome film. *Med. Radiog. & Photog.*, 1951, *27*, No. 4, 125.

Vol. 71, No. 5

PREVENTION OF AND LOCATING MISFILED FILM ENVELOPES

By ERNEST S. KEREKES, M.D.
TULSA, OKLAHOMA

NINE colors of adhesive tapes or paint, one *constant* color for each of the numbers 0 through 9, placed at specific locations on the visible edges of film envelopes not only tend to keep films from being misfiled, but also afford quick visual location of a misplaced jacket.

Using paints of various colors instead of tapes may prove to be as satisfactory and less expensive; tape has the advantage of giving additional strength at the edges of envelopes. Manufacturers of film envelopes might be able to furnish them prenumbered and color-coded.

In the diagram (Fig. 1) it is seen that the "singles" location requires the sequential use of all ten colors of tape, which does not add to visual clarity. If this "singles" position is omitted, the location system, as a whole, is good to within ten films, which can be easily thumbed through to locate a particular envelope.

A misfiled envelope can immediately be identified by its interruption of the band of color.

2917 South Boston Court
Tulsa, Oklahoma

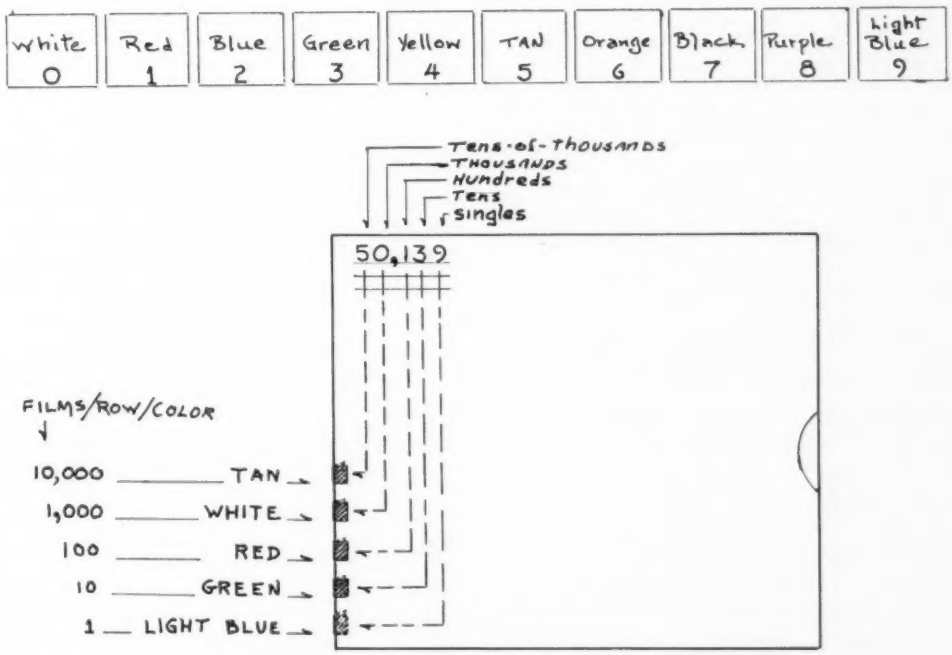

FIG. 1. Constant color per number is maintained in the department, as, for example, top row, 1 inch spacing between the colors on the jacket edge is recommended.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

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Associate Editors: Harry Hauser, M.D., Traian Leucutia, M.D., Russell H. Morgan, M.D., Edward B. D. Neuhauser, M.D., Wendell G. Scott, M.D.

Consulting Editorial Board: See front cover.

Published by: Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois.

Issued monthly. Annual subscription: United States, Mexico, Cuba, Central and South America, $15.00; Canada, $16.00; other countries, $17.00. Current single numbers, $1.50. Advertising rates submitted on application. Editorial office, 110 Professional Building, Detroit 1, Michigan. Office of publication, 301–327 East Lawrence Avenue, Springfield, Illinois. Information of interest to authors and readers will be found on page iv.

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Fifty-fifth Annual Meeting: Shoreham Hotel, Washington, D. C., September 21–24, 1954.

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Thirty-seventh Annual Meeting: 1955, to be announced.

EDITORIAL

THE ANNUAL MEETING OF THE AMERICAN RADIUM SOCIETY

THE Thirty-Sixth Annual Meeting of the American Radium Society was held at The Homestead, Hot Springs, Virginia, on March 14, 15 and 16, 1954. The variety and organization of the program and the attractive atmosphere of the hotel contributed greatly to the success of the meeting. The total attendance was 244, consisting of 84 members, 75 guests and 85 ladies. On the afternoon of the first day, the Society was welcomed by Dr. M. B. Jarman of Hot Springs. Dr. H. Dabney Kerr eloquently introduced Dr. Edith H. Quimby who delivered the Presidential Address entitled, "The Clinical Radiation Physicist—A Specialist within the Field of Radiology." This address was unique in that Dr. Quimby emphasized the importance of the physicist in the scheme of the specialty of medical radiology.

A new variation in the program was introduced by Dr. Richard H. Chamberlain of Philadelphia, who presented teams of collaborators of radiologists and physicists in the demonstration of radiological procedures. These demonstrations were given by means of explanations, instruments, animated models, graphs and lantern slides. The subjects discussed included correction of measurements of radium implants as projected on the roentgenogram, measurement of radioactive iodine before and after using tracer doses, calculation of isodose curves in several planes in the treatment of brain tumor, and the administration of radioactive colloidal gold.

The morning session of the second day, Monday, was devoted to clinical subjects relating to cancer and dermatological radiation problems. Dr. Paul E. Rekers of Los Angeles was moderator for an interesting symposium on "Cancer of the Lung" which included present day knowledge on pathology, surgery, conventional roentgen therapy and supervoltage roentgen therapy. Many questions were asked by members of the audience.

One of the more important events of the meeting was the Janeway Luncheon and Lecture held in the beautiful Empire Room of the hotel. Following remarks by Dr. Quimby concerning the history of the Janeway Lecture, Dr. Gioacchino Failla introduced in glowing terms the Janeway Lecturer, Dr. Lauriston S. Taylor, Chief of the Atomic and Radiation Physics Division, National Bureau of Standards, who spoke on "Education in Radiation Protection." Dr. Taylor stressed the importance of education of the younger radiologists in radiation protection so that they may be prepared to assume the responsibilities to themselves and others, and to play a decisive role in any legislation which may be necessary in the future.

The remainder of the scientific program was devoted to a variety of clinical, biological and physical subjects. In the morning session of the third day, Dr. Douglas Quick was moderator of a symposium on the "Treatment of Nasopharyngeal Neoplasms." Various modalities of radiation therapy were discussed by the participants of the panel.

On Sunday evening a social hour for members and guests was held in the Ball Room and was sponsored by the Radium Chemical Company of New York City. The Annual Banquet was held on Monday evening in the Empire Room. Dr. Quimby described the Janeway Medal, explained the meaning of its design, and presented it

to Dr. Lauriston S. Taylor in recognition of his outstanding work in the field of radiology. Dr. John A. Wall, Chairman of the Public Relations Committee, introduced the speaker of the evening, Dr. Francis P. Gaines, President of Washington and Lee University. The title of his address was "In Search of Life's Motive." He pointed out that the history of the world was built on defeated dreams in the minds of men and that the supreme test of an educated man was his sacrifice for an abstract idea.

The atmosphere of southern hospitality offered by The Homestead and the time of year made this meeting unusually successful from both the scientific and social aspect.

HARRY HAUSER, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Shoreham Hotel, Washington, D.C., Sept. 21–24, 1954.

American Radium Society
Secretary, Dr. R. E. Fricke, Mayo Clinic, Rochester, Minn. Annual meeting: 1955, to be announced.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: Biltmore Hotel, Los Angeles, Calif., Dec. 5–10, 1954.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois.

Section on Radiology, American Medical Association
Secretary, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual meeting: San Francisco, Calif., June 21–25, 1954.

Fifth Inter-American Congress of Radiology
General Secretary, Dr. Eugene P. Pendergrass, 3400 Spruce St., Philadelphia 4, Pa. Meets at Shoreham Hotel, Washington, D. C., April 24–30, 1955.

Alabama Radiological Society
Secretary, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

Arizona Radiological Society
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Atlanta Radiological Society
Secretary, Dr. Albert A. Rayle, Jr., 478 Peachtree St., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, October through April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. Elbert K. Lewis, 6337 S. Harvard Ave., Chicago, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

Cleveland Radiological Society
Secretary, Dr. Mortimer Lubert, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
Secretary, Dr. Parker Allen, Children's Hospital, Denver, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday October and April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. O. H. Grunow, 650 Fifth Ave., Fort Worth, Texas. Meets monthly, third Monday, at Greater Fort Worth International Airport at 6:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. F. Lang, Harper Hospital, Detroit, Mich. Meets monthly first Thursday, October to May, at Wayne County Medical Society Building.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. H. G. Reaves, Medical Arts Bldg., Sarasota, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. Robert M. Tankesley, 218 Doctors Bldg., Atlanta, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Greater Miami Radiological Society
Secretary, Dr. R. D. Shapiro, 541 Lincoln Rd., Miami Beach, Fla. Meets monthly at various South Florida Hospitals.

Houston Radiological Society
Secretary, Dr. Harry Fishbein, 324 Medical Arts Bldg., Houston 2, Texas. Meets fourth Monday each month at Hermann Hospital.

Idaho State Radiological Society
Secretary, Dr. Alfred M. Stone, St. Lukes Hospital, Boise, Idaho. Meets annually at same time as Idaho State Medical Association.

Illinois Radiological Society
Secretary, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

Iowa Radiological Society
Secretary, Dr. James T. McMillan, 1104 Bankers Trust Bldg., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary, Dr. A. M. Cherner, Hays, Kansas. Meets in spring with State Medical Society, and in winter on call.

Kentucky Radiological Society
Secretary, Dr. David Shapiro, 323 East Chestnut St., Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

Kings County Radiological Society
Secretary, Dr. Solomon Maranov, 1450 51st St., Brooklyn 19, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. George Jacobson, 1200 N. State St., Los Angeles 33, Calif. Meets second Wednesday each month at Los Angeles County Medical Association Building, Los Angeles.

* Secretaries of societies are requested to send timely information promptly to the Editor.

MAINE RADIOLOGICAL SOCIETY
Secretary, Dr. Jack Spencer, Maine General Hospital, Portland 4, Maine. Meets in early spring, June and fall.

MARYLAND RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. H. Leonard Warnes, 2337 Eutaw Place, Baltimore 17, Maryland.

MIAMI VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

MID-HUDSON RADIOLOGICAL SOCIETY
Secretary, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, September to May.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Hodgson, Mayo Clinic, Rochester, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

MISSISSIPPI RADIOLOGICAL SOCIETY
Secretary, Dr. John W. Evans, 117 N. President St., Jackson, Miss. Meets third Thursday of each month at the Rotisserie Restaurant at 6:30 P.M.

MONTANA RADIOLOGICAL SOCIETY
Secretary, Dr. Grant P. Raitt, Suite 413 Medical Arts Bldg., Billings, Montana. Meets at least once a year.

NASSAU RADIOLOGICAL SOCIETY
Secretary, Dr. Frank Huber, Hempstead, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. J. F. Kelly, Jr., 816 Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Stanley M. Wyman, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. J. R. Freid, 1049 Park Ave., New York 28, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Sternbergh, Charlotte Memorial Hospital, Charlotte, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY
Secretary, Dr. D. H. Baxter, Albany Hospital, Albany, N. Y. Meets in Albany area on second Wednesdays of October, November, March and April.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY
Secretary, Dr. H. B. Stewart, 2920 Capitol Ave., Sacramento, Calif. Meets at dinner last Monday of each month, September to June.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. M. M. Thompson, 316 Michigan St., Toledo, Ohio. Annual meeting, Toledo, Ohio, May 22 and 23, 1954.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Danstrom, Medical Arts Bldg., Oklahoma City, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. J. W. Loomis, 919 Taylor St. Bldg., Portland 5, Oregon. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse 416 Pine St., Williamsport. Next annual meeting at Bedford Springs Hotel, Bedford, Penna., May 14 and 15, 1954.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. H. M. Stauffer, Temple University Hospital, Philadelphia 40, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. Donald H. Rice, Western Pennsylvania Hospital, Pittsburgh 24, Pa. Meets 6:00 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Md. Meets third Tuesday each month, September to May, inclusive.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. William A. Goodrich, 85 Jefferson St., Hartford 6, Conn. Meetings are held bi-monthly.

RADIOLOGICAL SECTION, MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA
Secretary, Dr. A. C. Wyman, 5445—28th St., N.W., Washington, D. C. Meets Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
Secretary, Dr. Chapin Hawley, 927 Carew Tower, Cincinnati 2, Ohio. Meets monthly from September to June on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

RADIOLOGICAL SOCIETY OF HAWAII
Secretary, Dr. P. S. Arthur, Young Hotel Bldg., Honolulu 13, T. H. Meets third Friday of each month at a place designated by the Secretary.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA
Secretary, Dr. J. T. Brierre, 700 Audubon Bldg., New Orleans. Meets annually during Louisiana State Medical Society Meeting.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Salomon Silvera, 921 Bergen Ave., Jersey City, N. J. Meets at Atlantic City at time of State Medical Society and in November in Newark, N. J.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA
Secretary, Dr. Donald R. Laing, 65 N. Madison Ave., Pasadena 1, Calif.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Henry H. Forsyth, Jr., 40 Meigs St., Rochester, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. John H. Freed, 4200 East Ninth St., Denver 7, Colo.

St. Louis Society of Radiologists
Secretary, Dr. W. B. Seaman, 510 South Kingshighway, St. Louis 10, Mo. Meets fourth Wednesday each month, except June, July, August and September.

San Antonio-Military Radiological Society
Secretary, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets Brook Army Medical Center Officers Mess first Monday of each month.

San Diego Radiological Society
Secretary, Dr. C. W. Bruner, 2456 Fourth Ave., San Diego 1, Calif. Meets first Wednesday of each month at the University Club.

San Francisco Radiological Society
Secretary, Dr. I. J. Miller, 2680 Ocean Avenue, San Francisco 27, Calif. Meets quarterly.

Section on Radiology, California Medical Association
Secretary, Dr. H. R. Morris, 1027 "D" St., San Bernardino, Calif.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. George E. Irwin, Jr., 703 N. East St., Bloomington, Ill.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Bay Radiological Society
Secretary, Dr. J. J. McCort, Santa Clara County Hospital, San Jose, Calif. Meets second Wednesday each month.

South Carolina Radiological Society
Secretary, Dr. William A. Klauber, Self Memorial Hospital, Greenwood, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Tennessee Radiological Society
Secretary, Dr. G. K. Henshall, 311 Medical Arts Bldg., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May, Service Memorial Institute.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Eva L. Gilbertson, 1317 Marion St., Seattle 4, Wash. Meets fourth Monday of each month from September through May at 610 Pine St., Seattle.

West Virginia Radiological Society
Secretary, Dr. W. Paul Elkin, 515 Medical Arts Bldg., Charleston, W. Va. Meets concurrently with annual meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester Radiological Society
Secretary, Dr. C. G. Huntington, 170 Maple Ave., White Plains, N. Y. Meets on third Tuesdays of January and October and on two other dates.

Wisconsin Radiological Society
Secretary, Dr. W. W. Moir, 309 Geele Ave., Sheboygan, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
Secretary, Dr. Wm. W. Saunders, Veterans Administration Hospital, San Francisco 21, Calif. Meets monthly, third Thursday, at 7:45 P.M., Lane Hall, Stanford University Hospital.

Cuba, Mexico, Puerto Rico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexicana de Radiología, A. C.
Secretary General, Dr. Eugenio Toussaint, Calle del Oro No. 15, Mexico 7, D.F. Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. Rafael A. Blanes, Ave. Ponce de Leon 1175, Santurce, P. R.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86, Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

British Empire

Association of Radiologists of the Province of Quebec
Secretary, Dr. J.-P. Jean, 4039 Tupper St., Westmount, Que.

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. D. L. McRae, Suite 305, 1555 Summerhill Avenue, Montreal 25, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electro-Radiologie Médicales
General Secretary, Dr. Ls Ivan Vallée, 1058 rue St-Denis, Montreal 18, Canada. Meets third Saturday each month.

College of Radiologists (Australia and New Zealand)
Honorary Secretary, Dr. Alan R. Colwell, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W.

South America

Asociacion Argentina de Radiologia
Secretary, Dr. Lidio G. Mocsa, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Sociedad Argentina de Radiologia, Junta Central, Buenos Aires
Secretary, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Argentina de Radiologia, Filial del Litoral, Sede, Rosario
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

Sociedad Argentina de Radiologia, Filial del Sur, Sede, La Plata
President, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Centro Sede, Cordoba

President, Prof. Dr. David L. Caro, Corro 86, Cordoba. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Norte, Sede, Tucuman
President, Dr. Julio Mendez Valladares, Rivadavia 358 Tucuman. Meets monthly.

Sociedad Argentina de Radiologia, Filial de Cuyo Sede, Mendoza.
President, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Colombiana de Radiologia
Secretary, Dr. Luis E. Lozano B., Carrera 12 No. 20–69, 6° piso, Bogota, Colombia. Meets last Thursday of each month.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Société Française d'Electro-Radiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord
Secretary-General, Dr. A. Dariaux, 9 bis, Boulevard Rochechouart, Paris IX°, France.

Ceskoslovensk společnost pro rëntgenologii a Radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Deutsche Röntgen-Gesellschaft
Secretary, Dr. med. Peter Kröker, Evangelisches Krankenhaus, Huyssens Stiftung, (22a) Essen. Annual meeting, Sept. 5–8, 1954, Wiesbaden, Germany.

Societa Italiana di Radiologia Medica
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

Nederlandse Vereniging voor Electrologie en Roentgenologie
Secretary, Dr. B. J. Rethmeier, Bornsestraat 378, Almelo, Netherlands.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept.. Akademia Gdansk.

Wrocław Section Polish Society of Radiology
Secretary, Dr. R. Marciniak, Akad. Medyczna Wrocław, 68 Curie-Skłodowska St., Wrocław, Poland. Meets first Sunday of each month, X-Ray Department, Akademia Medyczna Wrocław.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

India

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

THE SOCIETY OF NUCLEAR MEDICINE

The first organizational meeting of The Society of Nuclear Medicine was held in Spokane, Washington, January 23, 1954. Twelve representatives from various areas in the Pacific Northwest were present.They elected an Executive Committee composed of the following: *President,* Thomas Carlile; *President Elect*, Asa Seeds; *Secretary*, Rex Huff, 2418 Harvard N., Seattle, Washington; *Treasurer*, Norman Holter. The first official annual meeting was scheduled for May 29 and 30, 1954, at the Benjamin Franklin Hotel, Seattle, Washington. The purpose of this organization is to promote discussion and communication of knowledge of nuclear phenomena, as they apply or are likely to apply to the understanding and control of disease.

Those interested in becoming charter members should make application to Milo Harris, 252 Paulsen Building, Spokane, Washington.

Abstracts for presentation for the first annual meeting should be sent to William H. Hannah, RR. No. 2, Box 896, Bremerton, Washington.

SYMPOSIUM ON FUNDAMENTAL CANCER RESEARCH

The Eighth Annual Symposium on Fundamental Cancer Research of The University of Texas, M. D. Anderson Hospital and Tumor Institute was held on April 5 and 6, 1954, in the institution's new building in the Texas Medical Center. Tissue culture in cancer research was the chief topic, and a number of papers were presented on this subject by various outstanding research workers from various parts of the country. The Tissue Culture Association, meeting at that time in Galveston, participated in the program of the first day.

On Monday night, April 5, a banquet was held at the Shamrock Hotel, and the Bertner Lecture was delivered by Dr. Peyton Rous, one of the nation's outstanding scientists, and an emeritus member of the Department of Pathology and Bacteriology of the Rockefeller Institute for Medical Research in New York. The Bertner Award in the form of a bronze medallion, was presented to Dr. Rous at this time.

On the afternoon of the second day, there was a joint meeting of the Anderson Symposium with the South Central Region College of American Pathologists and The University of Texas Postgraduate School of Medicine. This was a Cancer Pathology and Radiology Conference on Tumors of Infancy and Childhood, conducted by Dr. Edith Potter of Chicago, Illinois, and Dr. Frederick N. Silverman of Cincinnati, Ohio. The moderator of this conference was Dr. Wylie D. Forbus of Durham, North Carolina.

IRA I. KAPLAN LECTURE

At a meeting of the Bellevue Hospital Radiation Therapy Alumni Association to be held on Thursday, May 20, 1954, at the New York University College of Medicine at 2:30 P.M., the Annual Ira I. Kaplan Lecture will be delivered by Dr. Ira T. Nathanson, Associate Clinical Professor of Surgery, Harvard Medical School, Boston, Massachusetts. The subject of his lecture will be "Hormonal Therapy in Cancer of the Breast." There will be a discussion by Dr. Gray H. Twombly, Professor of Gynecology, New York University College of Medicine.

SYMPOSIUM NEURORADIOLOGICUM

The Fourth Symposium Neuroradiologicum will be held in London, England, under the presidency of Dr. James Bull, from September 13 to 17, 1955. Radiologists, neurosurgeons, neurologists and others interested will be most welcome. All those wishing to contribute papers are invited to communicate as soon as possible with the Honorary Secretary, Dr. R. D. Hoare, National Hospital, Queen Square, London, W.C.1, England.

KANSAS RADIOLOGICAL SOCIETY

At its recent meeting in Kansas City, Kansas, on February 15, 1954, the Kansas Radiological Society elected the following officers for the ensuing year: *President*, Dr. Willis L. Beller, Topeka Kansas; *Vice President*, Dr. G. Sherman Ripley, Salina, Kansas; *Secretary-Treasurer*, Dr. A. M. Cherner, Hays, Kansas.

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

Dedick, Andrew P., and Caffey, John. Roentgen findings in the skull and chest in 1,030 newborn infants. *Radiology*, July, 1953, *61*, 13–20.

The authors present the roentgen findings in lateral skull and posteroanterior chest roentgenograms of 1,030 newborn infants. Cases were selected at random, and all premature infants were excluded.

The nasal bones were not visible in 3 of the group. Clinical signs of mongolism were present in 2, and the third was suspected of being a mongol at birth, but was not seen later. In a series of 5,000 infants of which this study was a part, there were 8 with conclusive signs of mongolism. Mineralization of the nasal bones was present in 3 of these so that absence of mineralization of the nasal bone does not appear to be an invariable finding in mongolism.

An ossification center of the anterior arch of the atlas was present in 27 per cent of the cases. This occurred most frequently in white female infants. The older the mother and the heavier the baby, the greater was the incidence of the atlas center. Ossification centers were seen in the hyoid body and hyoid horns in 60 and 59 per cent respectively. The incidence was higher in white babies. Combination of ossification centers of both the hyoid body and hyoid horns was seen in 53 per cent, and one or the other alone in 7 per cent of cases. Centers were present in the hyoid body, hyoid horns, and anterior arch of the atlas in 18 per cent. The interparietal ossification center or centers were present in 12 per cent. The centers for the coracoid processes and humeral heads were, with one exception, present bilaterally. The coracoid processes were present in 20 per cent and the humeral heads in 18 per cent of all cases. A combination of the two was noted in but 5 per cent of all cases.

Accessory ossicles were found in the occipital bone in 0.8 per cent. It was believed that a Towne view would have shown a higher incidence .

Fractured clavicle was found in 12 cases, 8 on the right and 4 on the left. In this study all the fractures occurred in the vertex presentations. In only 1 instance was there difficulty in delivery of the shoulders. In 5 of the 12 cases, delivery was normal and spontaneous. The labors were not unduly long. Four of the 12 mothers were multiparas.

Ten of the series showed air-containing lung above the first rib. Herniation was bilateral in all cases. It is the authors' opinion that cervical herniation of the lungs during the first days of life is not significant clinically.—*Donald N. Dysart, M.D.*

Martin, F. A., Webster, J. E., and Gurdjian, E. S. The relative accuracy of electroencephalography, air studies and angiography in a series of two hundred mass lesions. *J. Neurosurg.*, July, 1953, *10*, 397–403.

Concise tabulation of the accuracy of the various modalities in the diagnosis of intracranial masses is presented. The relative value of each procedure in cases of neoplasms, hematomas and abscesses is considered. It is concluded that no single method is adequate for the localization of all types of intracranial mass lesions. The method of choice depends on the clinical concept of the site and the physical status of the patient.

Electroencephalography was found to be useful mainly as an adjunct in localizing supratentorial masses. False foci were found in 45 of 198 cases and in more than one-third of the sub-dural hematomas.

By carotid angiography it was possible to localize masses of the anterior two-thirds of the cerebral hemisphere, and about 50 per cent of those that occurred in the midline base. The authors consider this to be the preferred method in the severely ill patient with a pathologic condition suspected at these sites.

Pneumoencephalography was found to be successful in localizing 40 per cent of tumors of the hemispheres. Masses that occurred in the basal cisterns, an area that is not visualized by ventriculography, were also delineated by pneumoencephalography.

On the other hand, the authors believe that ventriculography is the method of choice in posterior fossa lesions or where intracranial hypertension is present. Ventriculography was found to be the most nearly accurate method available. It was possible to localize 75 per cent of hematomas and abscesses and 90 per cent of neoplasms with ventriculography.—*Thomas B. Efford, M.D.*

Terrafranca, Raymond J., and Zellis, Allan. Congenital hereditary cranium bifidum occultum frontalis; with a review of anatomical variations in lower midsagittal region of frontal bones. *Radiology*, July, 1953, *61*, 60–66.

The authors report 4 cases of cranium bifidum occultum frontalis occurring in three generations of a colored family. There have been few reported cases of cranium bifidum occultum frontalis as such, but many where this finding was associated with craniofacial dysostosis, cleidocranial dysostosis, or abnormalities of the central nervous system.

In the cases reported here, the cranium bifidum occultum frontalis was associated with large parietal foramina and spina bifida occulta, but the patients were otherwise normal. A discussion is presented on the development of the frontal bone.—*Donald N. Dysart, M.D.*

Reddy, D. Govinda, and Ramamurthy, B. Ventriculographic changes in cysticercosis of

the brain. *Brit. J. Surg.*, July, 1953, *41*, 11–12.

The authors present one case of central nervous system infestation by the larva of *Taenia solium*, which they were able to diagnose by filling defects protruding into the air-filled ventricles. Histologically, one of the nodules found at operation in the subcortical area of the left postcentral region showed a well-defined encysted scolex.

Occasionally, calcification of the larva may also be helpful in locating the lesion roentgenographically.

They state that epilepsy occurring in a patient with no family history of seizures in childhood and the presence of cysticerci in the subcutaneous tissue and somatic musculature strongly suggest or support the suspicion of brain involvement.—*Thomas B. Efford, M.D.*

Eisen, David. Cleidocranial dysostosis; with a report of four cases. *Radiology*, July, 1953, *61*, 21–31.

Cleidocranial dysostosis is a congenital abnormality of the skeletal system involving particularly bone of membranous origin. The pathognomonic findings are hypoplasia of the clavicles, increase in the transverse diameter of the skull, and delay in ossification of the fontanelles. Other changes which may also be present consist of faulty eruption of the teeth, scoliosis, poorly ossified pubic and ischial bones, failure of union of bones formed from more than one ossification center, and a few less consistent alterations. It is thought to be a disease with hereditary transmissions through both the male and the female, and a study of the records of families in which this abnormality appeared suggests that it tends to outbreed itself.

The author report 4 cases which will be added to the previously reported total of 323 cases. Three of these cases occurred in members of a single family—a father and his two children.—*Donald N. Dysart, M.D.*

Olsson, Olle. Vertebral angiography in cerebellar haemangioma. *Acta radiol.*, July, 1953, *40*, 9–16.

According to Lindau, hemangiomas of the cerebellum are small and well outlined. They are localized to the cortical or subcortical layer of the ventral or dorsal part of the cerebellum.

Tumors of this type are rarely multiple in the central nervous system, where they occur in the cerebellum and spinal cord. If they arise in the medulla oblongata, the dorsocaudal region is the site of election.

The author reports the roentgenologic appearance of 7 cases in which vertebral angiography was carried out.—*C. Peter Truog, M.D.*

Ethelberg, Sven, and Vaernet, Kjeld. The angiographic configuration of intracerebral metastatic tumors. *Radiology*, July, 1953, *61*, 39–48.

A study of 21 verified cases of carcinomatous supratentorial metastases is presented. In the majority of these cases, the tumor affected directly or was immediately subjacent to the cortex of the cerebral hemispheres. Multiplicity of the metastatic process was found at either operation or autopsy in 5 cases, although this was shown on the angiogram in only 1 instance. More than half the tumors affected the parieto-occipital regions of either hemisphere.

There appeared to be a certain definite relationship between the size of the metastatic tumor and its location. The nearer to the central or rolandic region, the smaller was the growth. Tumors in the occipitoparietal region and those of the extreme frontal location were the largest. This observation should be expected, since tumors in the central region should give rise to earlier clinical manifestations.

Common to the entire series was the fact that the tumor was localized in the terminal territory of a given artery, and the favorite location coincided with the area of brain supplied by the largest terminal branches of the internal carotid artery.

When endoneoplastic circulation could be demonstrated, this appeared as an almost circular opaque shadow in which no distinct vessel could be identified, or as a bundle of delicate arteries, circular or semicircular in course, surrounding an avascular area. In other cases, a small circular avascular area was found.

One or more delicate arteries supplying the tumor could be seen in all but 2 instances. Although in a few cases there was a definite enlargement of some of the supplying arteries, ordinarily no such enlargement was present.

The displacement of adjacent cerebral arteries was extremely localized and slight, and there was no change in the extracerebral vascular configuration.

In differential diagnosis, the angiographic findings in other types of tumors are discussed and compared with those seen in metastatic tumors.—*A. Ralph Watson, M.D.*

Neck and Chest

Robert, François, and Hoffmann, Theo. Zum Nachweis der Ösophagusvarizen und ihrer klinischen Bedeutung beim portalen Hochdruck. (Demonstration of esophageal varices and their clinical significance in portal hypertension.) *Fortschr. a. d. Geb. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1953, *79*, 51–70.

The authors use a new contrast material, carboxyethylcellulose barium mixture, which forms a thin coating on the mucosa. The patient takes a

teaspoonful of the mixture and exposures are made two to five minutes after swallowing it.

Four stages are differentiated in the development of varices:

Stage I. Diffuse venous hyperemia of the submucous plexus in the lower esophagus. Slight widening of the mucosal folds is seen.

Stage II. Dilatation of one or several submucous venous trunks causing disturbance of the normal mucosal pattern. The esophagus appears slightly dilated.

Stage III. Typical grape and worm-like mucosal pattern and arcade-like outline of the esophagus in its lower half.

Stage IV. Involvement of great lengths of the esophagus with dilatation of its lumen.

The pressure in the portal system was measured at the time of operation in 22 surgical cases and correlated with the roentgen appearance. It was found that esophageal varices always signify elevation of portal pressure, but the stage of varix formation is not always in direct relationship to the portal pressure since blood may be diverted through the anastomotic channels to a greater extent than through the esophageal plexus. This also holds true for the tendency to bleed. The patient's age, formation of other collateral channels, peptic ulceration and thrombotic changes in the varices are important factors.

Failure to demonstrate esophageal varices is a contraindication to surgery.

Careful examination of the esophagus for varices in all cases of unexplained gastrointestinal bleeding is advised. The differential diagnosis, pathology and treatment are discussed.—*Frederick M. Reis, M.D.*

Simpson, Ross J. Mediastinal foreign bodies; their treatment; an analysis of 32 cases. *Ann. Surg.*, July, 1953, *138*, 51–64.

The author points out that mediastinal foreign bodies, in and around the heart and great vessels of the chest, present a problem, not so much of diagnosis, as of treatment. It is his contention that such foreign bodies should be removed and he presents evidence in favor of a more radical approach to the problem.

He discusses the indications for removal of the metallic foreign bodies, after their implantation and after the patient has recovered from his initial injury. All of these patients had metallic foreign bodies consisting of missiles of war in or near the heart and great vesssels. No case was excluded for any reason. Sixty per cent of the patients were completely asymptomatic, and one-half of those with symptoms had minimal symptoms usually referable to pulmonary pathology. Seventy-four per cent of the patients were seen within ten days after injury. It was felt that the situation of these men was unstable because the foreign bodies may produce erosion with massive hemorrhage, infection with abscess, cellulitis in dangerous positions, embolism, either of the missile itself or of septic thrombi with severe systemic reaction.

Thirty-two patients had had foreign bodies in the mediastinal region. In this group of cases all primary pulmonary problems were eliminated and only those cases where the objects actually touched in some way the heart or great vessels were considered. The incidence of primary pulmonary foreign bodies on this service has been about 15 times greater than that of foreign bodies in the mediastinum.

The only mortality in the group was that of an officer admitted ten days after injury who presented a striking picture of a large hemothorax which masked a pericarditis, and a small foreign body was located close to the right auricle.

Complications were kept to a minimum with vigorous attempts at prevention rather than treatment. Atelectasis developed in one patient. The author feels that although thoracotomy is not a minor procedure in itself, with adequate facilities and trained personnel the danger is minimal and, in their experience, is far less than the potentiality of infection, erosion or embolism. The psychological effect on the soldiers was not definitely considered in the appraisal but it is pointed out that there was a great psychological relief when the patient saw his foreign body postoperatively.

The 32 cases are presented in detail and many are illustrated with photographs and roentgenographic reproductions.—*Robert D. Moreton, M.D.*

Amory, Harold I., and Sieber, Paul E. The supraclavicular shadows in chest film interpretation. *Radiology*, July, 1953, *61*, 8–12.

A heretofore unrecognized sign useful in recognition of lesions in the supraclavicular fossa is presented. The normal "supraclavicular shadows" are seen as sharp linear soft tissue lines which parallel the superior border of the clavicles and are continuous with the outer margins of the sternomastoid shadows. These lines are about 3 mm. above the clavicle and represent the skin edge dipping into the supraclavicular fossa. They may be discerned in 73–88 per cent of normal adults, but usually are not present in children and are never seen in infants.

Gross malposition, *marked sloping shoulders*, and particularly *obesity* (all of which are recognized on the film) have been observed to cause obliteration of these markings in normal persons. In almost every such case, the reason for the absence was obvious.

In absence of the supraclavicular shadow (especially if unilateral) without any apparent reason, the attention of the clinician should be directed to the area. Twelve cases of Hodgkin's disease, cancer or tuberculous adenitis are listed in which this sign was of diagnostic importance.

Thorough physical examination should reveal the masses, infiltration, or edema responsible for the shadows' obliteration, but at times they may be over-

looked. The sign is of value to the radiologist in obtaining a more accurate impression of the extent of a disease, such as lymphoma, and increasing the accuracy of his report. Its paramount use is probably in photoroentgen chest survey studies which do not include physical examination and often are done with the individual fully clothed.

When there is bilateral absence of the supraclavicular shadows without signs of obesity or other cause given above, one should be suspicious; *unilateral* obliteration should be considered abnormal.—*William A. Goodrich, Jr., M.D.*

MARDER, SUMNER N., and SCOTT, WENDELL G. The right anterior oblique projection in the angiocardiographic demonstration of infundibular stenosis. *Radiology*, June, 1953, *60*, 797–803.

Pulmonic stenosis is the most important single finding in evaluating patients with cyanotic congenital malformations of the heart for the selection of those who may benefit from surgical measures. Also an accurate delineation of the infundibular portion of the right ventricle with angiocardiographic studies may be of value in determining which operation the patient should have. The usual views employed in angiocardiography to "separate" the two sides of the heart are the left anterior oblique and the left lateral views. In some cases, however, opacification of the superior vena cava and/or the dextraposed aorta has interfered with an accurate visualization of the outflow tract of the right ventricle in these projections.

Because of the above situations the authors investigated and report their experience to date using the right anterior oblique projection which has been found to be of great value in providing unobstructed visualization of the infundibulum of the right ventricle and in visualizing the infundibular stenosis seen in the tetralogy of Fallot. They present 4 case studies in which biplane serial angiocardiographic studies were done. These studies provided simultaneous right-angle exposures in the right anterior oblique view and the left anterior oblique view. The authors have found that the degree of obliquity does not appear to be a critical factor and at the present time are using a 5 or 10 degree deviation from the true frontal and lateral projections with the higher degrees of obliquity being used in the older patients.

While this series of cases is small the results have been sufficiently accurate to recommend this technic for further clinical trial.—*Donald N. Dysart, M.D.*

DUBILIER, WILLIAM, JR., STEINBERG, ISRAEL, and DOTTER, CHARLES T. Kyphoscoliosis: angiocardiographic findings. *Radiology*, July, 1953, *61*, 56–59.

In kyphoscoliosis right heart failure occurs secondary to the pulmonary changes, which mainly are: areas of compression and emphysema and decreased lung volume due to the misshapen thorax. At postmortem, the typical changes of cor pulmonale are found in 75 per cent with this condition.

Roentgenographic changes in routine examinations are: cardiac displacement to the left in right scoliosis, prominent pulmonary artery segment and lack of prominence of aortic knob.

The authors report the angiocardiographic findings in 4 patients with severe right kyphoscoliosis, which are as follows: (1) the cardiovascular structures accommodate themselves to the deformity of the thorax; (2) there is a tipping without compression of the heart chambers and great vessels, and, if this is sufficiently severe, due to a shortened vertical axis of the thorax, the heart may become horizontal; (3) the heart is rotated to the right; (4) the superior vena cava goes direct to the right atrium without following the curvature of the spine; (5) the right and left pulmonary arteries are dilated and their branches conform to the misshapen lungs; (6) in emphysematous areas the peripheral branches are narrowed and separated with decreased blood flow; (7) the aorta closely follows the distorted spine; (8) identification of cor pulmonale is limited in angiocardiography.—*Dean Nichols, M.D.*

HEMLEY, SAMUEL D., SCHWINGER, AARON, and HARRINGTON, LEO A. Calcification of the left auricle. *Radiology*, July, 1953, *61*, 49–52.

The authors report 2 cases of calcification of the left auricle adding to the approximately 19 cases previously recorded in the world literature.

As in all the other reported cases a clinical or pathologic diagnosis of rheumatic heart disease was made. All cases were accompanied by auricular fibrillation, and the suggestion has been made that changes take place within the auricle proper with auricular fibrillation which in some way are responsible for the deposition of calcium salts.

Most cases can be diagnosed on ordinary posteroanterior teleroentgenograms although overexposed Potter-Bucky films will more clearly define the outlines of the calcifications. Typically a curvilinear calcification will be observed within the area of the left auricle.

The differential diagnosis includes coronary artery calcification, ventricular aneurysms, mitral and aortic valvular calcification, pericardial calcification, ecchinococcus cysts, calcified cardiac tumors, hilar lymph nodes and calcified costal cartilages.—*Donald N. Dysart, M.D.*

ZOLLINGER, H. U., and FISCHER, F. K. Weitere empirische und experimentelle Untersuchungen über die Joduron-Bronchographie. (Further empirical and experimental studies on ioduron bronchography.) *Schweiz. med. Wchnschr.*, July 11, 1953, *83*, 645–656.

Water soluble contrast material in bronchography has been found to be of practical value in recent years. The authors have noted no significant clinical damage to the lungs in over 2,000 bronchographies with ioduron B, carboxylmethylcellulose (CMC). Fischer has reported large granulomas in the lungs of 6 patients after bronchography with ioduron B.

The authors report on 100 cases of lobectomy or pneumonectomy after ioduron B bronchography in bronchiectasis, bronchogenic carcinoma, etc. The interval between bronchography and operation varied from twenty-nine hours to nine months. In only 5 cases, definite CMC residuals were noted. These were seen only in the abnormal portion of the lung, where diseased bronchi were located. The interval in these 5 cases was eleven to thirty days and it is possible that the granulomas which were found in these lungs might have regressed if a longer time had elapsed. The authors doubt, however, whether such lesions can disappear completely. One case of extensive granulomatosis with involvement of almost the entire lingual segment of left lung was noted among the 5 cases reported here. The other 4 cases showed little or no granulomatous reaction and are considered as retention CMC nodules. Study of the bronchograms of the 5 cases suggests that forced over-filling of the bronchi and alveoli may be the cause of the CMC retention.

This seemed confirmed by another case, in which deliberate over-filling was done, and laminagraphy three days later showed an infiltration in the lung segment previously outlined on the bronchogram.

Experimental Studies.

The object was to ascertain the frequency and morphology of CMC changes after ioduron B bronchography with forced injection as compared to normal injection of the bronchi. Thirty dogs were used and the results may be divided into 3 groups:

(1) Massive alveolar and bronchial filling—tiny CMC nodules scattered throughout the lungs.

(2) Clear filling of the larger bronchi—normal lungs, grossly and microscopically.

(3) Filling of the larger bronchi predominantly, with isolated peripheral areas outlined—few, tiny CMC nodules.

Films exposed four weeks after bronchography showed that in those dogs with intentional alveolar filling, there was a fine linear increase in the lung markings radiating from the hilus; in the other animals, the lungs were normal. It thus appears that with *bronchiolar* or *alveolar* filling with ioduron B, there is always a retention of CMC. The reaction is inflammatory in nature. Giant cells are few in number. The patency of the bronchus of the over-filled portion of the lung plays an important role in the retention of the CMC.

It is concluded that CMC reactions are seldom seen (5 per cent). Usually, simple retention nodules are found; thick granulomas are rare. When these reactions are noted, they produce no significant functional damage. The changes did not occur in normal lungs in the authors' series. Usually, they were seen in lungs with bronchostenosis, as in bronchogenic carcinoma.

Severe bleeding does not follow properly carried out bronchography with ioduron B. It is essential that over-filling of the lungs be avoided.—*Samuel Richman, M.D.*

Maier, Herbert C., and Gould, Wilbur J. Agenesis of the lung with vascular compression of the tracheobronchial tree. *J. Pediat.*, July, 1953, *43*, 38–42.

A case of agenesis of the lung is presented in which the cause of intermittent intense cyanosis was determined to be due to tracheal compression by the great vessels.

The infant was a premature female whose birth weight was 3 lb. 7 oz. At six weeks of age respiratory difficulty and chest wall retraction developed. Roentgen studies showed shift of the mediastinal structures to the right, opacification of the right hemithorax and herniation of the left lung across the midline. The esophagus was compressed in its upper thoracic segment. At ten weeks of age, because of increasing pressure on the trachea as manifested by severe cyanosis at the time of feeding and crying, exploratory thoracotomy was performed. No right pleural space or lung was found, and there was no evidence of a rudimentary bud from the trachea. The left pleural space extended to the mid-axillary line. The pulmonary artery was not seen. No cardiac abnormality was evident. The aorta, which was normal in size, passed anteroposteriorly to the left of the trachea, causing compression and marked displacement of that structure. An attempt to relieve the compression was made by freeing the arch of the aorta and crushing the right phrenic nerve.

The infant died on the first postoperative day. Autopsy substantiated the surgical findings and revealed that the left pulmonary artery crossed between the trachea and esophagus. Because of lack of distention of the vessels, compression of the trachea as evident at surgery could not be demonstrated at the postmortem examination.

Thus, the authors feel that the respiratory difficulty and death were caused by vascular compression of the airway by the aorta anteriorly and the pulmonary artery posteriorly.

Reference is made to case reports and analyses of agenesis of the lung as made by other authors.—*Doris E. Pipkin, M.D.*

Storey, Clifford F., Grant, Roald A., and Rothmann, Bruce F. Coin lesions of the lung. *Surg., Gynec. & Obst.*, July, 1953, *97*, 95–104.

Asymptomatic, small, solitary, circumscribed pulmonary lesions are encountered rather frequently

since the practice of routine chest roentgenography has been adopted. These coin lesions are becoming of increasing importance because: A significant per cent prove to be malignant; accumulated experience has shown that pulmonary tuberculomas, which most of these lesions prove to be, are best treated by resection; evidence indicates that such masses almost always warrant removal on their own merits if they are neither malignant nor tuberculous; and recent advances in anesthesia and thoracic surgery now make removal of this type of lesion a procedure of little risk.

The paper presents 40 consecutive cases of coin lesions in which the diagnosis was verified histologically. Exacting criteria are stated for the definition of a coin lesion, the purpose of which is to exclude Ghon tubercles, hilar and chest wall lesions, and large neoplasms.

Thirty-eight of the cases were treated by excision with the final diagnosis of tuberculoma in 70 per cent and carcinoma in 17.5 per cent. There was no surgical mortality and spread did not occur in any patient whose lesion was tuberculous. Surgical excision without undue delay is presented as the treatment of choice in patients with coin lesions of the lung.—*John F. Weigen, M.D.*

Hood, Robert T., Jr., Good, C. Allen, Clagett, O. Theron, and McDonald, John R. Solitary circumscribed lesions of the lung; study of 156 cases in which resection was performed. *J.A.M.A.*, July 25, 1953, *152*, 1185–1191.

This paper consists of a review of 156 patients with solitary circumscribed lesions of the lung who were subjected to surgical excision of the mass. Approximately 35 per cent of the lesions were malignant; the remaining 65 per cent were benign.

Roentgen examination of the chest served two important purposes. It was the sole means of detection. It was of diagnostic value in that every lesion in which calcification could be demonstrated proved to be benign. Laminagraphy was frequently necessary to visualize the calcification.

Evaluation of the various other diagnostic procedures employed in the study of these patients showed that only one was of absolute value—the cytological examination of the sputum. Although most of the lesions were peripheral and therefore unfavorably situated for the recovery of exfoliated cells, the diagnosis was established by cytological examination of the sputum in 53 per cent of the patients with bronchogenic carcinoma whose sputum was examined.

Two other diagnostic procedures were helpful. The sedimentation rate was frequently elevated in patients with malignant lesions but usually was not in those with benign lesions. The tuberculin test, when negative, increased the suspicion of a neoplasm.

The rest of the diagnostic procedures, including bronchoscopy, were noncontributory.

This study greatly simplifies the program for the patient with a solitary circumscribed pulmonary lesion. If calcification cannot be demonstrated roentgenologically, prompt surgical excision is indicated. For as complete preoperative evaluation as possible, the sputum should be examined adequately for malignant cells, the sedimentation rate and the tuberculin reaction should be determined. Further study and further delay, provided the patient is an acceptable surgical risk, are not warranted.—*George Cooper, Jr., M.D.*

Arrieta Sánchez, L. Triada de Kartagener (informe de un caso). (Kartagener's triad; report of a case.) *Radiología*, Panamá, June, 1953, *3*, 139–142.

Kartagener's triad consists of chronic sinusitis, situs inversus, and bronchiectasis. Kartagener presented 11 cases of this triad in 1933 and to date 40 other cases have been described in the medical literature.

The author reports the case of a seventeen year old youth who, since the age of one year, has suffered from a "catarrhal condition" (abundant nasal secretion, expectoration, frequent attacks of fever and cough). As a matter of fact, the patient never enjoyed good health and was always emaciated and anemic.

Roentgen examination showed dextrocardia and complete situs inversus of the digestive tract as well as of the liver; bronchiectasis in both bases; absence of the frontal sinus and bilateral cloudiness and infection of the maxillary antra. Bronchography demonstrated typical diffuse cylindrical bronchiectasis.

The diagnosis of bronchiectasis was confirmed by lobectomy. The pathologic study revealed extensive inflammatory peribronchial reaction and alternating zones with tendency to emphysema or to partial collapse.

The etiology of the triad is still a matter of discussion.

The author advises roentgen study of the bronchial tree as well as of the sinuses in all cases of situs inversus. Patients with situs inversus should avoid infections as much as possible as these infections may lead to bronchiectasis and sinus involvement.—*Ernst A. Schmidt, M.D.*

Cohen, Archibald C. Pulmonary moniliasis. *Am. J. M. Sc.*, July, 1953, *226*, 16–23.

Because *Candida albicans*, the etiological agent of moniliasis, may often be recovered from the mouth, throat, skin, intestinal tract, and vagina of healthy persons and from the sputum of patients known to have tuberculosis, lung abscess, bronchiectasis, pulmonary carcinoma, and other chronic lung

diseases, the diagnosis of pulmonary moniliasis is justified only if the organism can be recovered regularly from fresh sputum or from specimens obtained through the bronchoscope and if all other possible etiological agents are excluded.

Although some are still skeptical that pulmonary moniliasis occurs other than as a secondary infection, reports of primary moniliasis, especially in the American literature, are accumulating more and more rapidly. It is possible that antibiotics, by inhibiting the bacterial portion of the flora, are given the fungi opportunity for more luxuriant growth. Monilial infections are usually not severe, but a few serious infections of the lungs, heart, and other internal organs have been reported.

The clinical picture of pulmonary moniliasis is not specific. In mild cases, cough and expectoration may be the only symptom. In severe cases, to these symptoms may be added hemoptysis, dyspnea, chest pain, weakness, weight loss, fever, and night sweats.

Roentgenograms show no diagnostic changes. Hilar and peribronchial thickening with patchy parenchymal infiltration are usual. Sometimes small cavities appear.

Since the treatments of pulmonary tuberculosis and moniliasis are different, patients with active, progressive disease should not be treated for tuberculosis merely because the chest roentgenogram is consistent with tuberculosis. If the sputum is negative for acid-fast bacilli, sputum or bronchoscopic specimens should be cultured repeatedly for fungi.

When a diagnosis of moniliasis is made, the patient should be skin-tested to determine whether he is hypersensitive to *Candida albicans*, and if he is, he should be desensitized. If he is not, or if he has been desensitized, iodides in large doses will usually be successful. Sometimes intravenous gentian violet is helpful.—*George Cooper, Jr., M.D.*

Kugel, E., Harlacher, A., and Hueck, O. Bemerkungen zur Differentialdiagnose und Therapie der Lungenaktinomykose. (On differential diagnosis and therapy of pulmonary actinomycosis.) *Thoraxchirurgie*, Aug., 1953, *1*, 206–214.

Primary pulmonary actinomycosis is rare and since it presents no characteristic roentgenologic or clinical signs, the differential diagnosis from tumor, tuberculous or nonspecific narrowing of the bronchi is often impossible, except after resection of the affected lung segment.

Early diagnosis, however, is important if one is to institute successful therapy by conservative measures. The more advanced cases with their extensive and serious changes such as abscesses, bronchostenosis and secondary bronchiectases require a combination of surgical and conservative means of treatment.

Five cases of pulmonary actinomycosis are presented in detail. Two of these had lung resections for suspected lung cancer and 1 for lung abscess. Another patient had a minor operation on the chest-wall which revealed actinomycosis, and the last case was treated with penicillin only. All 5 cases were cured.

The mode of infection and bacteriology are discussed. Bronchoscopy, bronchial washings and bronchography do not help in the diagnosis and resection is usually necessary.—*Frederick M. Reis, M.D.*

Hutchison, H. E., and Fraser, K. Pulmonary adenomatosis. *Brit. J. Surg.*, July, 1953, *41*, 1–5.

The authors give a brief résumé of alveolar cell tumors, a group which includes pulmonary adenomatosis.

They found 62 cases of pulmonary adenomatosis in the literature up to 1949. The disease is characterized by abundant, clear, frothy sputum and most patients have been between forty and sixty years of age. Hemoptysis is not uncommon. Clinically and roentgenologically patchy areas of consolidation, which tend to coalesce and become lobar, eventually involving the entire lung, are found. Coalescence of the densities may result in a roentgen appearance not unlike that seen in primary atypical pneumonia or mycosis. Cytologic examination of the sputum may be of value in diagnosis.

Since it is unknown whether the lung is involved by extension or by multifocal origin of pulmonary adenomas, the correct therapeutic approach is difficult to determine. It is therefore uncertain that the disease will ultimately prove amenable to surgery. Because of the rapidly progressive course, the authors believe that a logical approach would be to perform radical surgery before the lesion becomes widespread and irradiation in instances so extensive that excision of a single area would not help the total situation.

Histopathologically pulmonary adenomatosis is locally malignant. Progressive pulmonary insufficiency is frequently the cause of death.

The authors present a case which following lobectomy revealed roentgenologic evidence of involvement of the other lung and the patient succumbed in six months. Histopathologically the surgical specimen indicated the diagnosis of pulmonary adenomatosis. No necropsy was obtained.—*Thomas B. Efford, M.D.*

Abdomen

Lidl, H. Über die röntgenologische Prüfung der Fettaufbereitung im Magen-Darm-Trakt. (The roentgenologic determination of fat digestion in the gastrointestinal tract.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1953, *79*, 70–79.

Fat digestion in the small intestine was determined by an ingenious method of using specially prepared barium balls covered with fat. After the fat coating is digested, the barium sphere becomes indistinctly outlined and disintegrates. Three to five such balls are ingested and spot films made at one-quarter to one hour intervals.

In normal individuals the barium balls remain unchanged in the stomach and disintegrate in the small intestine after an average time of three hours. An elapsed time of four hours or longer is abnormal as is that of two and one-half hours or less. Digestion in the stomach takes place only when there is regurgitation from the duodenum. In a stenosed duodenum no digestion is observed because of low concentration of digestive juices. In a few normal cases no digestion takes place until the barium is in the lower ileum but the fat is readily digested there. After rapid passage through the upper small intestine the transit through the lower small intestine is slowed down by a compensatory mechanism. Normal motor function of the small intestine is of great importance for normal digestion. With normal motility and normal gallbladder function, cases of gastric and duodenal ulcers show normal fat digestion as do those with hypersecretory gastritis. The results in achylia gastrica are inconclusive.

Gastric resections (Billroth II) with rapid passage through the upper small intestine show delay in fat digestion. Billroth I type of resections show normal digestion because of slower transit time through the upper small intestine. The transit time through the proximal small intestine and especially the duodenum is of prime importance for proper fat digestion, provided there is an adequate quantity of digestive juices.

Great delay in digestion is seen in cases with nonvisualized gallbladders. Normal digestion is present in cholecystectomy cases while in cases with icterus the barium passes into the colon unchanged.

While this paper deals mostly with determinations of fat digestion in normal cases, the author plans to investigate cases of tuberculosis, hyperthyroidism and hypothyroidism, enteritis, diabetes and dystrophies.—*Frederick M. Reis, M.D.*

Hutchison, John, and Thomson, J. D. Congenital archenteric cysts. *Brit. J. Surg.*, July, 1953, *41*, 15–20.

The authors give a brief review of the reported cases of epithelial-lined cysts related to the gastrointestinal tract.

A case report of an eighteen year old woman with a congenital epithelial-lined cyst of the mediastinum is presented. The cyst extended from the neck to the diaphragm and had a fistulous communication with the esophagus which was believed to have been the site of an old ulceration in the cyst.

Surgical excision was performed in two stages: the first, by a thoracic approach, and the second, through a neck incision. Histologic examination revealed the cyst to contain both gastric and intestinal mucous membrane.

The authors discuss the embryologic development of the gastrointestinal tract and the possible etiology of the cysts. They favor the term archenteric cyst as the most appropriate name for this condition, since these cysts may display a variegated pattern reflecting all the developmental potential of endodermal tissue.—*D. V. Campbell, M.D.*

Palmer, Eddy D. An attempt to localize the normal esophagogastric junction. *Radiology*, June, 1953, *60*, 825–831.

The exact localization of the esophagogastric junction is more complex than once believed. Whatever the external appearance may be, any portion of the gullet which is lined by gastric mucosa must be considered stomach, because it functions as stomach, and is heir to the ailments which afflict that organ.

Anatomically, the only clear-cut indication of the limits of the distal esophagus is the uneven line marking the abrupt termination of the squamous epithelium. Neither the abrupt increase in the digestive tube's diameter at the stomach nor the obliquity of the esophagogastric junctional angle can necessarily be accepted as indications of the actual beginning of the stomach.

The present study was made in an effort to localize the esophagogastric epithelial junction roentgenographically. Esophagoscopy was carried out in 15 normal subjects. Biopsy was taken and a silver clip was attached to the line of the junction of esophageal and gastric mucosa.

On upright examination, in all cases, the clip lay somewhere between the left border of the spinal column and a point 3 cm. to the left of this as observed on posteroanterior studies. The location of the clip when studied during deep inspiration was seen to vary between a level opposite the lower border of T-8 and the upper border of T-11. The relationship of the epithelial esophagogastric junction of the lumen's abrupt dilatation into the stomach proper was controlled in part by the volume of the contents of the gastric fundus. When the stomach was largely empty, the gastric mucosa was found to extend as far as 3 cm. up into the "esophagus," and when the gastric fundus was distended moderately, the junction was drawn toward the brink of the stomach proper. Lateral view showed that the position of the junction shifted anteriorly no more than 1 or 2 cm.

On fluoroscopic examination it was observed that, from time to time, mysterious spontaneous migrations of the clips toward and away from the stomach proper occurred. These excursions extended about 2 cm. in most patients. These could not be correlated with the ampullary emptying, the degree of filling of the most distal esophageal segment, respiratory motions, or other evidence that either active or

passive longitudinal shortening of all esophageal layers was occurring. The appearances were clearly those of a mobile mucosa which was propelling itself over the deeper tissues, presumably due to contraction of the muscularis mucosae.

The implications of mucosal mobility and automotion at the cardia may be considerable. Some instances of peptic ulceration, adenocarcinoma, erosive gastritis, adenoma and retrograde mucosal prolapse would have to be considered in the light of a sliding mucosa.—*A. R. Watson, M.D.*

Dodd, Gerald D., Fishler, James S., and Park, Oakley K. Hyperplasia of Brunner's glands; report of two cases with review of the literature. *Radiology*, June, 1953, *60*, 814–821.

The authors report 2 additional cases of hyperplasia of Brunner's glands which were clinically detected and demonstrated on roentgen examination. The diagnosis is made when gastric hyperacidity is found in the presence of roentgenologically demonstrable multiple duodenal nodules, in a patient with a vague history of abdominal distress conforming to no specific pattern.

The literature is reviewed and the condition is discussed in relation to carcinoma and the secretory function of the glands. The authors believe this hyperplasia is a protective phenomenon against gastric hyperacidity, that it is a benign process, and that surgical resection is not indicated.—*Everett E. Seedorf, M.D.*

Aye, Ralph C. Peptic ulcers in children; with report of four cases. *Radiology*, July, 1953, *61*, 32–38.

The literature is reviewed and 4 new cases of peptic ulcer in children are reported. Attention is called to the fact that peptic ulcer in children is not as uncommon as was once thought. The proportion of duodenal to gastric ulcers has been given by various authors as 3 to 1 to 7 to 1. Forty-five cases of gastric ulcer have been reported in children between the ages of three months and fifteen years. The three year old gastric ulcer patient in this series is the forty-sixth of this age group, and the tenth less than six years old.

The number of chronic ulcers is not nearly so great as the total number of ulcers, and the great majority of peptic ulcers occurring in the first months of life are acute.

The etiology of peptic ulcers is unknown. Most authors believe emotional trauma unimportant in the child. All patients in this series had emotional difficulties.

The younger the child, the more obscure the signs and symptoms. In the 4 patients here reported, the most common presenting complaint was abdominal pain. Other signs were tarry stools, vomiting, and nausea.

Differential diagnosis includes mesenteric adenitis, appendicitis, volvulus, intussusception, and acute pyelonephritis. Of greatest value is the realization that peptic ulcers do occur in infants and children.

Perforation heads the list of complications. Fifteen of the 46 cases of chronic gastric ulcer in children have perforated. Hemorrhage and pyloric stricture are other serious sequelae.—*A. Ralph Watson, M.D.*

Lopes Pontes, J. P., and Caminha, Nicola. Estudo radiológico do intestino delgado na hipertensão porta. (Roentgen study of the small intestine in portal hypertension.) *Rev. brasil. med.*, April, 1953, *10*, 231–238.

In view of the fact that the venous plexus originating from the small intestine contributes to a large degree to the total blood carried to the portal vein and is thus highly significant for the digestion and general nutrition, it is surprising that little research has been done and only few observations have been published concerning the role of the small intestine in cases of portal hypertension.

The authors performed roentgen examination of the small intestine and of the gastrointestinal tract in general in 12 cases of cirrhosis of the liver with symptoms and signs suggestive of portal hypertension. In 10 of these cases, changes in the appearance and motility of the small intestine were noted; in 5 the changes were rather advanced and in the remaining 5 they were less pronounced but still definitely pathologic. In some of the cases the changes were highly suggestive of organic alterations of the small intestine, especially edema or atrophy. In 1 case these organic alterations were confirmed by autopsy. In the majority of cases, the barium passage was accelerated in the jejunum and in the proximal portion of the ileum, whereas it was delayed in the terminal ileum. Occasionally, acceleration of the barium passage was also noted in the colon. Some of the patients showed very rapid barium passage throughout the whole gastrointestinal tract with total or almost total evacuation of the barium in less than three hours. In the more advanced cases, there was more or less marked obliteration of the mucosal relief, often combined with narrowing of the jejuno-iliac loops.

The histologic examination in the 1 case in which autopsy was performed showed atrophy of the ileum and of the jejunum with edema and leukocytic infiltration of the submucosa. Pronounced edema was also noted in the serosa, occasionally with a certain dissociation of the fibers and with thinning of the tunica muscularis.

The barium column was segmented presenting the well known "sausage" appearance. Its distribution was fine and discrete (appearance of "snow flakes") or clumpy and irregular. In many cases it was im-

possible to distinguish the functional disturbances in the contour and lumen from the actual organic changes.

According to the authors, the factors responsible for the pathologic changes shown in the roentgen examination of the small intestine are (1) venous stasis, (2) nutritional deficiency and (3) hypoproteinemia. However, the present study did not establish any definite relationship between the degree of reduction of blood proteins and the roentgen changes. —*Ernst A. Schmidt, M.D.*

CLAYTON, R. S., and THORNTON, W. L. Benign duodenocolic fistula; review of the literature and case report. *Radiology*, June, 1953, *60*, 832–836.

The authors report a case of benign duodenocolic fistula, making a total of 19 cases reported in the literature.

Since more cases have been demonstrated by barium enema than by upper gastrointestinal examination, it is concluded that the barium enema study should be done first. Determination of whether the underlying process is benign or malignant can be accomplished only by surgical exploration. The surgical treatment is described.—*Everett E. Seedorf, M.D.*

GLIDDEN, SAWYER A., and STAUFFER, HERBERT M. Pneumatosis cystoides intestinalis in an adult; preoperative roentgen diagnosis. *Radiology*, June, 1953, *60*, 822–824.

Pneumatosis cystoides intestinalis is a rare entity characterized by the presence of gas-containing cysts in the wall of the bowel. A case is reported which was diagnosed roentgenographically and confirmed on surgical exploration. In the roentgenogram, the cystic collection of pneumatosis may be seen anywhere in the abdomen, but the most common appearance is multiple small cysts scattered along the bowel. The gas may assume radiolucent stripes along the bowel margin or double ring shadows when the bowel is seen on end, due to radiolucency of the gas in the bowel wall surrounding the gas-filled lumen.

In discussing the etiology, it is thought that the condition is produced purely by mechanical factors which are described.

The condition is considered clinically unimportant, but must be differentiated from pneumoperitoneum. —*Everett E. Seedorf, M.D.*

HUNTER, HARRY L., and RAPP, ROBERT. Symptomatic hepato-diaphragmatic interposition of colon. *Radiology*, July, 1953, *61*, 67–70.

The causes of hepatodiaphragmatic interposition of the colon are enumerated and discussed.

The case of a thirty-four year old female is presented. She had suddenly developed a pain in the right upper quadrant of the abdomen which radiated to the right scapula and shoulder. Frontal roentgenograms disclosed the unusual appearance of the colon interposed between the right side of the diaphragm and the liver. During a barium enema study the patient was rotated to a prone position when a sudden descent of the hepatic flexure occurred, and the interposition of the colon disappeared. With this the patient obtained complete relief of her symptoms.—*Everett E. Seedorf, M.D.*

GAEBEL, EVA, and TESCHENDOFT, WERNER. Darstellung der Gallenwege mit Biligrafin (Schering); unblutige Cholangiographie. (Visualization of the biliary ducts with biligrafin [Schering]; bloodless cholangiography.) *Röntgen Blätter*, July, 1953, *6*, 162–170.

By the usual intravenous and oral methods of cholecystography the bile ducts are only occasionally visualized. Cholangiography can be carried out only as a result of an operative procedure or by filling of the duct system in retrograde fashion from the duodenum. In an attempt to find a medium which would allow "oral" cholangiography, the Schering Company of Berlin has prepared "biligrafin" which is a compound containing three iodine atoms per molecule [sodium N, N′-adipin-di- (3-amino-2,4,6-triiodobenzoic acid)]. Up to now contrast media for cholecystography have contained only two iodine atoms per molecule of compound. The first investigations with this contrast medium were performed by Frommhold and his results were presented at the meeting of the Rhine-Westphalian Roentgen Society on May 16, 1953. He reported the innocuousness of the material in animals and humans and presented over 250 clinical studies. His studies showed that the gallbladder shadow appeared very quickly ("rapid cholecystography") and the gallbladder filled with contrast medium usually by two hours.

The authors believe that the oral method with biliselectan (priodax) is in general satisfactory for visualization of the gallbladder itself and that this new contrast medium should be employed for study of the biliary tree. Biligrafin must be very concentrated in order that the biliary tree be visualized and therefore double the amount is used for visualization of the biliary duct than when the gallbladder alone is visualized. The injection of 40 cc. of biligrafin intravenously must be done over a twenty minute period (8–10 minutes per 20 cc. ampule); slower injection leads to insufficient concentration of the medium in the biliary ducts. Severe secondary reactions do not occur; nausea and vomiting have been encountered following rapid injection of the medium.

The clearest view of the biliary duct system is obtained ten to forty minutes after completion of the intravenous injection of the medium. The authors

prefer to position the patient under fluoroscopic control, thus avoiding overlap of the common duct and the spine.

Visualization of the bile ducts by this method is not as rich in contrast as by the operative methods, but is usually good enough for diagnosis of stone or other pathologic changes in the bile duct system. The medium is particularly useful in cholecystectomized patients to demonstrate remnant of the gallbladder and duct system.

The indications for use of the new medium are listed by the authors as:

1. In investigation of the cholecystectomized patient with symptoms suggesting disease of the bile ducts—stone, inflammatory process, gallbladder "regeneration," or odditis.

2. In cases where oral cholecystography shows gallbladder calculi and there is a question of calculi in the bile ducts. Included are all cases in which colic has occurred.

3. In cases where oral cholecystography yields negative results, intravenous biligrafin may visualize a stone.

The advisability of the use of the new medium in cases of hepatic insufficiency or jaundice has not yet been decided. In those cases where it has been tried, the medium has been excreted through the kidneys instead of the liver, and the pyelocalyceal system of the kidneys visualized fairly well. The appearance of the medium in the urinary tract or small intestine may lead to confusion.—*Harold Fulton, M.D.*

Albot, Guy, and Toulet, Jacques. La colecistografía de frente y de perfil en decúbito dorsal (método Albot-Toulet). (Frontal and profile cholecystography in dorsal decubitus; method of Albot-Toulet.) *Prensa méd. argent.*, July 3, 1953, *40*, 1673–1685.

Anteroposterior and lateral views with the patient in dorsal decubitus position are utilized before and after the fatty meal in cholecystography. The profile views not only reveal layering of stones, as previously described in upright and lateral decubitus positions, but also give, with the frontal views, a clearer idea of the volumetric and axis changes during the course of cholecystography. The latter are important in evaluating functional, nonlithiasic disorders of the biliary system, such as the hypotonic and hypertonic dyskinesias. The effects of localized inflammatory changes, as in the cystic duct, may also be seen.—*Charles M. Nice, Jr., M.D.*

Lapointe, Henri. Chronic cholecystitis and Rokytanski-Aschoff sinuses. *J. Canad. A. Radiologists*, June, 1953, *4*, 45–46.

The visualization of Rokitansky-Aschoff sinuses during cholecystography is quite a rare occurrence; the condition is usually seen only by the pathologist.

These sinuses consist of hernia-like protrusions of the gallbladder mucosa through its muscular layer and constitute "intramural diverticula."

In 495 gallbladders studied by Robertson and Ferguson of the Mayo Clinic diverticula existed in 93 per cent of the chronically inflamed gallbladders and were quite exceptional in gallbladders before the age of thirty.

This individual case report is that of a male, aged forty, who complained of vague digestive distress of two years' duration with loss of weight, asthenia, fatigue, and epigastric pains radiating to his back or in girdle fashion. The only positive findings were increased blood cholesterol level (4.49 gm. per cent) and two calculi by cholecystogram. The Rokitansky-Aschoff sinuses were quite visible on the five hour film and appeared as a chain of pearl-like shadows around the contour of the gallbladder lumen. The pathologist confirmed this finding after the gallbladder was excised. This case is the only one with associated lithiasis.

The question arises as to why not more than 7 cases of this condition have been reported in the literature, especially since the sinuses exist almost constantly in chronic cholecystitis. This is probably due to smallness of the sinus orifices, thickness of the bile, cholesterol deposits, lack of five hour film, failure to give a fatty meal, type of contrast media used, failure to examine in an oblique position, and misnomers of interpretation such as emphysema or intramural diverticula.—*John F. Berry, M.D.*

Nurick, A. W., Patey, David H., and Whiteside, C. G. Percutaneous transhepatic cholangiography in the diagnosis of obstructive jaundice. *Brit. J. Surg.*, July, 1953, *41*, 27–30.

Roentgenological demonstration of the biliary duct system apart from operation has not been generally regarded as practicable. Cholangiograms have been obtained by injection of contrast media into the gallbladder under peritoneoscopic control but the attempts were not followed up, probably because the danger of biliary leakage was too great. In 1952, Carter and Saypol described a case of obstructive jaundice in which cholangiograms were obtained by puncture of the left lobe of the liver under general anesthesia, and injection of the contrast medium after identifying an intrahepatic biliary duct by aspiration.

The authors have used this method in 4 cases of obstructive jaundice and in 3 nonjaundiced control cases. In all 4 cases of obstructive jaundice, good diagnostic cholangiograms were obtained, but no diagnostic visualization was accomplished in the 3 cases in which jaundice was not present, including a patient in whom the liver was needled at operation.

The following technique was used for the proce-

dure, which was performed on in-patients in the roentgen department after a preliminary injection of morphine: After local anesthesia of the puncture site with 2 per cent novocain, a 12 cm. needle, 1 mm. in external diameter, was inserted into the liver through a point in the anterior abdominal wall close to the right costal margin and 1½ to 2 inches from the ensiform cartilage. The needle was passed backward, slightly upwards and to the right until it was felt to enter the liver and this was confirmed by noting that the needle moved with respiration. The stylet was removed and a 20 ml. syringe containing saline was connected to the needle by a rubber tube with adaptors. The needle was then slowly advanced with an assistant maintaining suction on the syringe and if a portal vein was entered the blood was washed out by injecting a little saline and suction was maintained during withdrawal of the needle. If no bile was detected the needle was reinserted in a slightly different direction.

Bile was usually aspirated at a depth of 5 to 7 cm. from the skin. When a bile duct had been located, a few milliliters of 35 per cent diodone were injected and a check roentgenogram made to confirm filling of the biliary tree. Twenty milliliters of 35 per cent diodone was then injected slowly under fluoroscopic control and the needle withdrawn. A series of roentgenograms was then made, including some in the erect posture.

The reproductions of the roentgenograms in the patients with jaundice show the dilated biliary ducts well filled down the point of obstruction, which was on a malignant basis in all cases. One patient developed intraperitoneal bleeding and biliary leakage following the procedure, which led to his death. The authors felt this was due to lack of preparation with vitamin K and to the fact that two injections were done two days apart, 21 ml. diodone being used for the first and 40 ml. for the second injection. In all of the other cases the puncture site in the liver closed promptly with no bleeding or extravasation of bile.

The authors advise that all jaundiced patients should be prepared with vitamin K and transhepatic cholangiography should not be performed until the prothrombin readings are within normal limits. The amount of diodone injected should be limited to 20 ml. The negative results in the control cases suggest that without the dilatation of the intrahepatic ducts due to chronic obstructive jaundice, filling and visualization of the biliary system are unlikely.

It is believed that the dangers of bleeding and biliary leakage are no worse with transhepatic cholangiography than with liver biopsy, already an accepted procedure. The test is worth cautious further exploration in chronic jaundice; in obstructive jaundice it will confirm the diagnosis and establish the site and probable nature of the obstruction.—*A. B. Smith, M.D.*

Genitourinary System

Edling, Nils P. G. The radiologic appearances of diverticula of the male cavernous urethra. *Acta radiol.*, July, 1953, *40*, 1–8.

One must separate diverticula due to cyst formation of the bulbo-urethral ("Cowperian") ducts from those caused by a congenital disturbance in the closure of the urethral channel. The former are situated in the posterior portion of the cavernous urethra, while the latter, which are rare, are situated in the penile urethra. In either type they arise from the inferior surface of the urethra.

The roentgenologic findings in diverticula of the urethra with opaque medium are described.—*C. Peter Truog, M.D.*

Cammenos, A. L'urographie intramusculaire chez le nourrison et l'enfant (Hyaluronidase et Diodone). (Intramuscular urography in sucklings and infants; hyaluronidase and diodone.) *J. d'urol.*, 1953, *59*, 505–510.

In infants intravenous urography is often accomplished with difficulty because of the problem of venipuncture in this age group. To avoid this difficulty various routes of administration of the urographic medium have been suggested—oral, rectal, subcutaneous, intramuscular, and transosseous (intramedullary). None of these methods can replace the intravenous administration, because of their relative complexity of application and, more important, because generally less satisfactory urograms are obtained. The basic fault of these alternate routes is that absorption of the contrast medium is relatively slow and consequently concentration in the urinary tract proportionately diminished.

The problem has been resolved with the discovery of hyaluronidase. Hyaluronidase is an enzyme which penetrates the tissues and augments their permeability by its action on the intercellular binding substance (hyaluronic acid). Hyaluronidase accelerates considerably the resorption of contrast substances introduced into the subcutaneous or intramuscular tissue, and permits a renal concentration of iodine comparable to that obtained following intravenous injection of iodine-containing contrast substances.

Most workers have employed the subcutaneous administration of various contrast media combined with hyaluronidase. The subcutaneous injection in two to four different points is required, because of the relatively low tolerance of the subcutaneous tissue for contrast materials requires the dilution of the substance in large quantities of liquid diluent, the injection of which causes tension pain at the injection sites. To overcome this inconvenience the author injects all of the medium undiluted into a single intramuscular site. The results of this method have

been satisfactory and local tolerance to the media has been "perfect."

After preparation of the bowel and sedation of the infant, 150 T.R. units (Turbidity Reduction Units) of hyaluronidase diluted in 2 cc. of physiologic saline are injected in the upper outer quadrant of one buttock. Ten minutes later at the point of the hyaluronidase injection 35 per cent diodone in a quantity which varies with the age of the patient is injected. The prescribed doses are:

Age	*Dose*
Below 12 months	7–11 cc.
1–3 years	11–14 cc.
4–6 years	14–17 cc.
7–8 years	17–20 cc.

The dose of diodone is thus approximately 1 cc. per kilogram of body weight.

After the injection of the contrast medium the region of injection is massaged lightly to favor absorption.

The number of urographic films exposed varies with each patient, but generally the first is exposed 7–10 minutes after diodone injection, others every 15 minutes up to 55 minutes. The best excretion occurs between 22 and 40 minutes. Ureteral compression by band or balloon is recommended.

Cammenos insists on the ten minute interval between the two injections. Early in his experience with the method the contrast medium (diodone) was injected immediately after the hyaluronidase through the same needle which was left *in situ* in the gluteal muscle. The resulting urograms were satisfactory, but it was learned that hyaluronidase exerts its maximum spreading factor action at a pH of between 4.5 and 7 and that diodone solution has a pH of about 7.3. It seemed better, therefore, not to mix the two substances. Improved urograms resulting from the technique of ten minute interval between the two injections seem to bear out the logic of this step in the author's opinion.—*Harold Fulton, M.D.*

Skeletal System

Kerr, John G. Scoliosis with paraplegia. *J. Bone & Joint Surg.*, July, 1953, *35-A*, 769–773.

Forty-seven cases of scoliosis with paraplegia have been reported in the literature, indicating the extreme rarity of the condition as compared with the total cases of scoliosis seen throughout the world. In the case reported in this paper, the deformity was due to von Reklinghausen's disease. The author regards it as of special interest since complete recovery from paraplegia was attained as a result of spine fusion alone. He thinks it is difficult to explain the rapid and complete recovery of the paraplegia following the spine fusion. It is possible that the dissection in the concavity of the curve, although minimal, effected sufficient loosening of taut structures to allow slight correction of the curve.

It has been shown by McKenzie and Dewar that, in idiopathic scoliosis with paraplegia, laminectomy and decompression of the cord will suffice. However, in scoliosis associated with such conditions as osteogenesis imperfecta or neurofibromatosis, affecting the bone, it is felt that fusion is imperative if progress of the scoliosis is to be checked and further cord pressure prevented. In these and similar conditions, if the associated paraplegia is incomplete and of only short duration, the author suggests that a preliminary fusion in the concavity of the curve may be safely tried. Should no recovery occur in the paraplegia, decompression of the cord may then be done with the knowledge that no increase in the degree of curvature is to be anticipated.—*Ralph S. Bromer, M.D.*

Garceau, George J. The film terminale syndrome (the cord-traction syndrome). *J. Bone & Joint Surg.*, July, 1953, *35-A*, 711–716.

This paper is a report of observations made during the study and treatment of 3 patients presenting the symptoms of a progressive spastic paralysis. A tight filum terminale may cause the cord-traction symptoms known as the Arnold-Chiari syndrome. The associated pathological lesions were different in the 3 cases reported in the paper. In the first patient the tight filum terminale had prevented the distal migration of the spinal column, so that the conus medullaris had retained the fetal position. Paralysis occurred during the period of the rapid growth of the patient. In the second case, one of tuberculosis of the spine, the signs and symptoms of paraplegia developed during the period of rapid growth. Recovery followed sectioning of the filum terminale. Exploration at the area of kyphosis failed to reveal the cause of the paralysis. In the third case, that of a patient with idiopathic thoracolumbar scoliosis, the filum separated 1 cm. when sectioned, indicating the tightness of the structure. Almost complete recovery followed sectioning of the filum. The first 2 patients were each thirteen years of age. the third was fifteen.

The cord-traction syndrome has been associated in reports in the literature with simple spina bifida occulta, meningocele, myelomeningocele, diastematomyelia, congenital scoliosis, Klippel-Feil syndrome, cranium bifidum, tight fibrous bands, and bony spicules. All of these conditions may be associated with congenital deformities, especially in the lower extremities. These are usually evident at birth. The neurological abnormalities may be progressive.

The author states that his treatment of these patients could be questioned. Decompression of the foramen magnum could have given the same result. He is following his patients and thinks that he may later find that foramenotomy will be necessary.—*Ralph S. Bromer, M.D.*

Burman, Michael. Primary torsional fracture of the radius or ulna. *J. Bone & Joint Surg.*, July, 1953, *35-A*, 665–674.

This paper is a discussion of the primary torsional fractures of the radius and ulna which follow an externally applied torsional force, together with comments on secondary torsion of the radius by muscle pull. Four situations of torque as described by the author are possible: 1. The radius undergoes non-axial torsion. 2. The radius is twisted non-axially, but the ulna is twisted axially at about the level of the radial fracture. 3. The radius is held fixed and the force of torque is expended on the ulna, which is axially twisted and broken spirally. 4. The force torques the two bones as if they were one. These four situations are discussed fully in the paper with illustrative drawings and roentgenographic reproductions.

Roentgenographically, Burman states, it is easy to distinguish primary torsional fracture from the secondary form. In primary torsional fracture, the fracture line of the radius is spiral and the fragments are separated slightly. The radius is angulated to the ulnar side. There is no cross-sectional incongruence since the line of break is not transverse. The fracture of the ulna is likewise spiral, but whereas the radius turns non-axially, the ulna can only turn axially. Whether the fracture is old or recent, torsion is recognized by the change in relation between intrinsic bony landmarks.

In secondary torsional fracture, the fracture line is not spiral. There is cross-sectional incongruence and change in the relation between intrinsic bony landmarks. The degree of ulnar angulation of the radius is less, for less of a cone is swept out. The author defines the cone as the physiological cone generated by the revolution of the mechanical triangle of the forearm, illustrated by his drawings.—*Ralph S. Bromer, M.D.*

Barr, Joseph S., Elliston, William A., Musnick, Henry, Delorme, Thomas L., Hanelin, Joseph, and Thibodeau, Arthur A. Fracture of the carpal navicular (scaphoid) bone; an end-result study in military personnel. *J. Bone & Joint Surg.*, July, 1953, *35-A*, 609–625.

This paper is the report of an end-result study of 44 veterans who had fractures of the carpal navicular, recognized in Military Service during World War II. Each man was studied by a professional team consisting of an orthopedic surgeon, a roentgenologist, a psychiatrist, and a doctor interested in muscle physiology. A careful history was taken and compared with the information recorded in the health and hospital charts. This was followed by a physical examination, psychiatric evaluation, ergographic studies and a detailed roentgenographic examination.

The following conclusions were warranted from the study:

1. If healing by primary union occurs, there is minimal residual disability which does not interfere with the performance of duty.

2. About 50 per cent of the ununited fractures were surveyed from the Service for wrist symptoms. If the nonunion was present before induction, this injury should be disqualifying for full-duty status.

3. The incidence of nonunion in Military Service was 22 per cent. The factors tending to produce nonunion appeared to be insufficiently prolonged immobilization and delay in instituting treatment. Immobilization must be maintained until there is union as shown by roentgen examination. This may require more than eight weeks, even in acute fractures promptly diagnosed and treated.

4. The treatment of nonunion in this series was unsatisfactory. Of the 14 men with nonunion, 9 were treated conservatively without improvement; 5 were operated upon, union and a satisfactory result being obtained in two.

5. Persistent nonunion results in partial absorption, displacement and fragmentation of the fragments, cyst formation in the navicular, and degenerative arthritic changes. Functional impairment was present in every case, but earning power was impaired in only 42 per cent of the cases.

6. A psychiatric study of these patients revealed personalities to be heterogeneous with no particular trait outstanding. In only 6 instances were there clearly discernible psychological factors related to the fracture or the veteran's adjustment following the fracture.

7. The work capacity of these injured wrists, as determined by a specially designed recording ergograph, in cases with primary union showed little or no impairment. Only 1 of the 14 wrists with nonunion showed a normal work capacity. The ergographic tracing in the uncooperative patient was characteristic and proved to be an aid in detecting lack of cooperation.

The paper is illustrated with reproductions of roentgenograms of the wrists of some of the cases.—*Ralph S. Bromer, M.D.*

Christophe, Kenneth, Howard, Louis G., Potter, Theodore A., and Driscoll, Arthur J. A study of one hundred and four consecutive cases of fracture of the hip. *J. Bone & Joint Surg.*, July, 1953, *35-A*, 729–735.

This article presents a study of 104 consecutive cases of fractures of the neck of the femur. The majority of the fractures in the series were treated by internal fixation, with the aid of either Smith-Petersen cannulated nails or Smith-Petersen nails with Thornton plates. All patients were followed at least nine months, 64 patients were followed for three years or more and 6 were followed for ten years.

In 13 patients nonunion occurred and in 16, aseptic necrosis of a varying degree developed. Analysis of all cases of nonunion and aseptic necrosis suggested that incomplete reduction with persistent varus deformity was the commonest cause of poor results. Overcorrection with the head in a valgus position did not necessarily ensure union as has been suggested by some observers. The authors' study suggests that obliquity of the fracture line may require open reduction for accurate reduction and fixation. Union occurred in 70 of the 83 patients available for evaluation.—*Ralph S. Bromer, M.D.*

Adams, Raymond J., and Chandler, Fremont A. Osteitis pubis of traumatic etiology. *J. Bone & Joint Surg.*, July, 1953, *35-A*, 685–696.

In their review of the literature, the authors found indications that osteitis pubis is considered by the majority of investigators to be an inflammatory disease of bacterial origin, which occurs most commonly in males following retropubic surgery. Adams and Chandler believe that heretofore this disease when occurring in young adults of both sexes following trauma to the symphysis pubis may have been overlooked in reporting cases. They quote Henderson in describing the roentgenographic changes in osteitis pubis in patients following operation: In Stage 1 there is no abnormality or slight fraying of the corners of the symphysis. In Stage 2, there is definite decalcification of the bodies of the pubes which may be uniform or patchy and may involve one or both inferior rami. In the third stage. decalcification may continue till a U-shaped defect is seen at the site of the pubic symphysis. In the fourth stage, exceptionally the process is associated with sequestrum formation. In the fifth stage at first there is recalcification with normal trabecular conformation, and eventually marked narrowing or fusion of the symphysis takes place. New subperiosteal bone may be laid down in the region of muscle attachments. The last stage may require two years for completion.

Changes of similar nature may also be seen concomitantly in the ischial tuberosities, in which case the stage of healing is often accompanied by deposition of subperiosteal bone. In addition to involvement of the pelvic girdle it has been emphasized that narrowing of the hip joints, though rare, may sometimes be noted following an attack of osteitis pubis.

A case following trauma is reported, the patient being an eighteen year old male, who developed symptoms following running on an indoor track at high school. The sections removed were suggestive evidence that the traumatic disease involving the symphysis was inflammatory in nature and was very possibly of bacterial origin. The roentgenograms showing the course of the disease are reproduced.—*Ralph S. Bromer, M.D.*

Winkler, Harry. Old subluxation of the knee. *J. Bone & Joint Surg.*, July, 1953, *35-A*, 755–757.

The author states that a search of the literature on the specific treatment of old, chronic subluxation of the knee joint failed to reveal a description of a lesion similar to the one he presents in this paper. Dislocation and subluxation of the knee are relatively rare. Most textbooks describe an anterior, a posterior and a lateral dislocation. The old unreduced type offers a very poor prognosis as regards joint function, and will usually require fusion. He thinks it very likely that, if the subluxation in his case had been completely reduced, it would not have presented the clinical picture he describes in his case.

His patient, aged twenty-nine years, had, when operated upon, an unreduced dislocation of the right knee for eleven years. The initial cause was a severe trauma which occurred when she was struck by an automobile. Roentgenograms showed marked posterior displacement of the femur on the tibia with a lesser degree of lateral displacement. After two operations the dislocation remained reduced, and eight months after the second operation, the patient was walking without crutches and had flexion of 100 degrees.—*Ralph S. Bromer, M.D.*

Spigelman, Louis. Positive pressure in the reduction of fractures of the tibial condyles; a preliminary report. *J. Bone & Joint Surg.*, July, 1953, *35-A*, 696–700.

In this paper, a method is described of applying positive pressure to plateau fractures of the tibia. Tension of a simple internal cantilever spring maintains the positive pressure. The requirements for this method are a Moore pin, 3/32 inch in diameter and 5 inches in length, and a nut and orthopedic drill, pliers and a mallet. The procedure is explained by line drawings and illustrative roentgenograms of 1 of the 3 cases in which the method was used. In the first 2 cases, the casts were removed approximately ten days following the operation at which time the patients were permitted to move the knee freely. The first 2 patients were both back at work in approximately ten weeks, with an almost complete range of normal motion.—*Ralph S. Bromer, M.D.*

Hermel, M. B., and Gershon-Cohen, J. The nutcracker fracture of the cuboid by indirect violence. *Radiology*, June, 1953, *60*, 850–854.

This type of fracture, caused by the indirect application of force to the bone, has seldom been mentioned in the literature. Five cases are here presented, with a discussion of anatomic and physiological aspects.

The nutcracker fracture is produced when the weight of the body is transmitted to a foot held in exaggerated plantar flexion, with the anterior foot

fixed in position. The cuboid is crushed between the calcaneous and the bases of the last two metatarsals. —*Lynne J. Taylor, M.D.*

Vaughan, W. H., and Segal, G. Tarsal coalition, with special reference to roentgenographic interpretation. *Radiology*, June, 1953, *60*, 855–863.

Tarsal coalition is the union of two or more of the tarsal bones. Calcaneonavicular bar and talocalcaneal bridge are two of the more common varieties, though fusion between other bones can occur. These abnormal unions may be complete or incomplete, fibrous, cartilaginous or bony. They may be associated with pain and a "rigid flatfoot" or may be asymptomatic.

Calcaneonavicular bar is a congenital connection from the medial portion of the head of the calcaneus obliquely across to the adjacent lateral aspect of the navicular. It is best seen on the oblique views of the tarsus. Several slightly varying oblique projections may be necessary to clearly demonstrate the region.

Talocalcaneal bridge is a fusion which may be complete, but is more commonly partial, and is generally at the sustentaculum tali or medial aspect of the joint. The subastragalar joint is best seen on the lateral ankle view and on the "coalition view" which is made with the beam directed at a 45° angle posteriorly through the calcaneus with the patient standing on the film. Obliteration of this joint is diagnostic. An osteoarthritic spur at the talonavicular joint is often found in subtalar fusion. Repeat examinations for better position may be necessary.

Treatment consists of heel lifts, arch supports, and rest in mild cases. Triple arthrodesis is reserved for severe incapacitation. Surgical excision of the uniting segment is unsatisfactory.

Twenty-one cases in young soldiers are reported, with an incidence of about 1 per cent in patients complaining of painful feet. These patients were ultimately returned to limited duty or discharged.—*William A Goodrich, Jr., M.D.*

Thompson, William F. Blastomycosis of bone; report of a case. *J. Bone & Joint Surg.*, July, 1953, *35-A*, 777–781.

North American blastomycosis (Gilchrist's disease) is an uncommon fungous disease occurring rarely in New England, its geographic distribution being chiefly in the midwestern and southern portions of the United States. The case reported in this paper is of special interest since the patient had spent his entire life in New England and he has had apparently complete recovery from the disease. His case was one of systemic blastomycosis involving bone and which by history probably arose from the respiratory tract. The patient was treated with large doses of potassium iodide with apparently complete recovery.

Roentgenograms of the right foot showed a punched-out area of bone destruction in the calcaneus and an area of bone destruction in the medial condyle of the left femur. Roentgenograms made one and one-half years after treatment revealed healing of the lesions. On admission, the roentgenograms of the lungs showed fibrosis at the left base suggestive of old infection without evidence of active pulmonary disease. The diagnosis was established by examination of permanent section of the biopsy. Sections showed blastomycetes in the process of budding, which differentiates the disease from coccidioidomycosis, a condition in which endospores are found. No endospores were found in the case reported.

Roentgenographically the appearance of a lesion is usually that of a well defined punched-out area with little surrounding bone reaction.—*Ralph S. Bromer, M.D.*

Achenbach, W., and Böhm, A. Skelettveränderungen bei parathyreogenen Tetanien. (Skeletal changes in parathyrogenous tetanies.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1953, *79*, 95–103.

Skeletal changes in hypoparathyroid tetany are not common and not uniform. Increased bone density and increased calcium deposition are the outstanding findings. Demineralization, however, may be seen in the same cases and may be the dominant feature in rare instances. These cases must then be differentiated from those of hyperparathyroidism, vitamin D and AT-10 intoxication.

Disturbance of ossification is found when the alterations begin in the growth period. Small stature, growth lines, brachydactyly, short phalanges, and disturbance of dentition are other findings.

Calcification in the brain stem, choroid plexus, blood vessels and skin, trophic disturbances of the skin and its appendages and low mentality are also described in this entity.

One case is reported in detail, followed by a discussion of the literature, pathogenesis and treatment. —*Frederick M. Reis, M.D.*

Trueta, J. Acute haematogenous osteomyelitis: its pathology and treatment. *Bull. Hosp. Joint Dis.*, April, 1953, *14*, 5–23.

This is a brief account of the author's experience with combined penicillin and surgical therapy in 100 cases of acute hematogenous osteomyelitis (average duration of symptoms, four days) during the period 1944–1950. The cogent clinical facts are:

1. The disease predominates in children of average age ten or eleven years. "A first attack of acute hematogenous osteomyelitis is rare after the cessation of growth." Males outnumber females, 2:1.

2. *Staphylococcus aureus* is by far the most frequent offending organism (84 of 100 patients).

3. The tibia (34 cases), femur (25), fibula (10), and

humerus (10) account for 79 of the total 107 bone lesions encountered.

4. Forty-five per cent had ascertainable primary focus of infection, most of these being boils or infected abrasions. In 37 per cent there was some associated trauma to the bone just preceding the onset of symptoms.

5. The major diaphyseal nutrient arteries are the obvious route of implantation. Only 14 per cent presented themselves with complicating joint involvement in addition to a bone lesion.

6. At least thirty days' hospitalization was necessary in most cases, principally to insure adequate penicillin therapy.

Dr. Trueta and collaborators are engaged in a well-known research into the blood supply of bone, and the rationale of treatment is based upon his impression that chronic sepsis will develop if any delay in treatment permits the spreading infection to cause ischemia. "We are of the conviction that chronic osteomyelitis is more an ischemic disease of bone than a chronic sepsis; and we believe that persistent sepsis occurs in the bone only where the blood flow therein has substantially decreased." This has "convinced us that early *surgery* is essential in the treatment of acute osteomyelitis to prevent the disease from becoming chronic."

Penicillin 1,000,000 units per day (in three hour divided doses or constant drip, both given intramuscularly) is used to control the medullary portion of infection in the early lesion. But edema is beginning to compress surrounding vessels and cause ischemia within a few hours after implantation of the organisms. In the face of ischemia, the antibiotic cannot reach the involved cortex and periosteum. When edema and pus begin to strip up the periosteum, a rupture of periosteal arterioles is in sight. "To a cortex already suffering from ischemia due to loss of its central blood supply from the nutrient and perforating arteries, a rupture of the periosteal arterioles amounts to a calamity."

Therefore, early operation is the routine treatment in conjunction with penicillin. A simple periosteal incision is made to evacuate subperiosteal pus and fluid and permit re-apposition of periosteum to cortex. The underlying cortex may also be perforated to evacuate pus and edema fluid. The skin incision is then meticulously sutured without any drainage.

Results of this rapidly instituted combined program of simple surgery and antibiosis were most satisfying. Only 5 per cent developed sequestra; 95 per cent of patients recovered full function. Only 7 per cent developed limb shortening, mostly infants with epiphyseal involvement. This contrasts with the high incidence of shortening which used to occur following radical diaphysectomy.

However, 32 patients developed eventual lengthening of the extremity due to "a rearrangement of the blood supply following a thrombosis of nutrient vessels." This amounted to only a few millimeters in most cases, but was greater in the younger patients, as might be expected.

The roentgenographic end results were excellent in 66 per cent, with complete normal or only minimally abnormal bone appearance. The 12 per cent poor roentgenographic results were, again as expected, in infants and late-treated cases. Twenty-nine per cent of the patients received sulfonamides along with penicillin, and these individuals seemed to recover somewhat more quickly.—*Stanley M. Rogoff, M.D.*

Cullinan, Edward R. Scleroderma (diffuse systemic sclerosis). *Proc. Roy. Soc. Med.*, July, 1953, *46*, 507–511.

Diffuse systemic sclerosis rather than scleroderma is the term given to an uncommon condition in which there are generalized changes in the extremities early, and later systemic changes in other parts of the body including the alimentary tract, lungs and heart.

The author describes the clinical findings and course of this condition in 14 women ranging in age from thirty-three to seventy-one years. The onset as a Raynaud's phenomenon occurred as early as at twenty-three years of age. The hands were first involved, later the feet and other systems of the body became affected.

In the areas affected by acrosclerosis, pain and stiffness may lead to confusion with rheumatoid arthritis, although there is no real association with that disease.

Symptoms of gastrointestinal involvement were common, occurring in 10 per cent of 14 patients. They usually consisted of loss of appetite, flatulence, fullness after eating, heartburn and vomiting. Difficulty in swallowing was the most frequent and earliest symptom. Four cases are reported in detail.

No cure is known; however, temporary relief was obtained.—*V. L. Peterson, M.D.*

Harper, R. A. Kemp. The radiological manifestations of diffuse systemic sclerosis (scleroderma). *Proc. Roy. Soc. Med.*, July, 1953, *46*, 512–522.

The roentgenological findings of systemic sclerosis are characterized by atrophic changes in the distal end of the terminal phalanges with deposition of amorphous calcium in the soft tissue. In addition, calcium deposits may be seen at points of pressure such as about the elbow and along the ischial tuberosities.

The esophagus loses its tone and there is an irregular dilatation; similar changes are present throughout the intestinal tract producing pseudodiverticula due to loss of muscle in the wall of the intestinal tract.

There is a fibrosis in the alveoli and bronchi of the lungs with secondary cystic changes. These lead to cardiac enlargement, especially of the right ventricle.

Fluid is often found in the pericardium and pleural space at autopsy and may be demonstrated on fluoroscopic and reontgenographic examination.

The changes are described and illustrated and their frequency assessed.—*V. L. Peterson, M.D.*

Blood and Lymph System

Lin, Paul, Murtagh, Frederick; Wycis, Henry, and Scott, Michael. Carotid angiography with urokon, using the Chamberlain bi-plane stereoscopic angiographic unit; report of one hundred cases. *J. Neurosurg.*, July, 1953, *10*, 367–372.

Using the Chamberlain bi-plane stereoscopic angiographic unit with two Fairchild rapid-sequence roll-film cassettes, the authors performed 100 carotid angiograms in 72 patients using 30 per cent urokon. With this apparatus, 12 stereoscopic exposures in both anteroposterior and lateral views were made in 8.4 seconds, providing accurate timing of cerebral circulation. However, the films cannot be viewed for twenty minutes following exposure—a disadvantage if extravasation of contrast medium is suspected. Percutaneous injection was satisfactory in all but 3 cases. Sedation and local anesthesia were employed in the majority of conscious patients; uncooperative cases received intravenous pentothal.

Sensitivity to urokon was not discovered by preliminary intravenous injections of 1–2 cc., or by eye tests in 50 per cent of the cases. One complication occurred after 10 cc. of urokon, characterized by transient unconsciousness, hypotension, and precordial pain. Recovery in ten minutes was not followed by any apparent sequelae. Angiograms of this case showed a prolonged arterial phase, possibly due to vascular spasm from irritation by urokon, or arteriosclerosis.

The authors conclude that 30 per cent urokon compares favorably with 35 per cent diodrast in cerebral angiography, with milder subjective complaints following urokon injection.—*J. Maurice Swain, M.D.*

Sossai, Michele. Aortografia transcarotidea; studio anatomo funzionale della stenosi dell'istmo aortico e del dotto arterioso pervio. (Transcarotid aortography; an anatomical functional study of the stenosis of the aortic isthmus and of the patent ductus arteriosus.) *Ann. radiol. diag.*, 1952–1953, *25*, 417–430.

Since these two conditions are amenable to surgical intervention an accurate diagnosis becomes imperative. Transcarotid injection is preferred by the author. This is done under general anesthesia and surgical exposure of the craotid artery by inserting a catheter into the artery. The left carotid artery is utilized to opacify the descending arch of the aorta whereas the right side injection is preferred when the ascending portion of the arch is to be studied.

Thus coarctation of the aorta is best visualized when the right common carotid is injected. In cases in which a patent ductus arteriosus is suspected, injection of the left side is recommended. In about 10 per cent of the patients with coarctation of the aorta, a patent ductus arteriosus is also found.

The collateral circulation which develops in cases of coarctation is very well explained in this article together with the cause for notching of the inferior borders of the ribs. The extent of the collateral circulation depends on the degree of stenosis of the aortic isthmus and also on the duration of the disease. Thus patients over twenty years of age should show the changes of the ribs. The advantages to the surgeon in locating and determining the extent and degree of stenosis are stressed.

The number of cases examined in this manner is not recorded in the article but one death in a forty-five year old woman is reported. The author recommends that this procedure not be taken too lightly as it is not without some danger to the patient. In cases of patent ductus arteriosus cardiac catheterization is also utilized.—*Peter E. Russo, M.D.*

Burucúa, J. E., Perosio, A. M., Kaplan, S., Martiarena, L., and Suárez, D. Z. Fistulas arteriovenosas (estudio fisio patológico). (Arteriovenous fistulas; physiopathologic study.) *Prensa méd. argent.*, July 17, 1953, *40*, 1842–1848.

The authors describe 6 cases of arteriovenous fistulas, either solitary or associated with other vascular malformation. In 1 case an arteriovenous aneurysm was observed in the frontal region; in a second case an arteriovenous aneurysm was seen in the left hand. The third patient showed an arteriovenous fistula, apparently congenital, of the right upper extremity; the fourth patient a congenital arteriovenous fistula in the right hand. The fifth patient had a diffuse angiomatosis of more than one-half of the body, probably combined with a congenital arteriovenous fistula in the pelvis and upper part of the left lower extremity. In the sixth patient, an arteriovenous fistula was seen in the left hand.

As a constant diagnostic element, the blood of the efferent veins of the zone of the fistula shows a considerably higher oxygen content than the blood of the homologous and symmetrical veins of the other half of the body. In the opinion of the authors, this observation has a diagnostic value comparable to that of angiography, while the examination is much simpler and less hazardous as any accidents due to idiosyncrasy to the contrast medium are eliminated. This method can also be applied in the so-called essential varices which according to some investigators are real arteriovenous fistulas. The coefficient of the utilization of the oxygen is also analyzed as well as the variations of the arteriovenous pressure, the cardiac frequency and other aspects of the hemorespiratory function at rest, after exercise, and

before and after occlusion of the fistula. As only a slight increase in the size of the heart silhouette is noted, generally cardiac fluoroscopy is sufficient in the patient and no roentgenography of the heart is necessary.—*Ernst A. Schmidt, M.D.*

Perry, S. Paul, and Massey, Charles W. Bilateral aneurysms of the subclavian and axillary arteries; report of a case. *Radiology*, July, 1953, *61*, 53–55.

By means of arteriography the authors demonstrated bilateral aneurysms of the subclavian and axillary arteries in a fourteen year old white male. They believe this represented a congenital anomaly.

The patient complained of headaches and some blurring of vision of two months' duration. He had been under observation for hypertension, but his blood pressure was normal at the time of this examination. Four years previously he had a blood clot involving the left arm. Arteriography also demonstrated the site of this old thrombosis.—*Everett E. Seedorf, M.D.*

Gay, Brit B., Jr., and Walker, J. Franklin. Aneurysm of the innominate artery; review of clinical and radiologic findings in 18 cases. *Radiology*, June, 1953, *60*, 804–813.

Although aneurysms of the innominate artery have been known for centuries, this location is an uncommon site with only about 3 per cent of all aneurysms occurring here. Syphilis is the most common etiologic agent, the pure arteriosclerotic aneurysms being extremely rare.

The authors present an analysis of a series of 18 cases stressing the clinical findings and emphasizing particularly the roentgenologic methods of diagnosis.

The clinical findings encountered were largely dependent upon the pressure phenomena resulting from expansion of the vascular mass. The more common ones consisted of pain, pulsatile right anterior cervical mass, dyspnea, hoarseness, cough, dysphagia, venous congestion of face and neck and pupillary abnormalities.

Roentgenologically the diagnosis was made on routine roentgenographic studies and fluoroscopic examination, with angiocardiographic studies being confirmatory to the other methods.

Routine posteroanterior roentgenograms usually revealed a soft tissue density in the right paratracheal region arising at the level of the aortic arch. Peripherally distributed calcium deposits were seen occasionally in the mass. Tracheal displacement, bone erosion and calcification in the ascending aorta were also noted. Examination in the lateral and left anterior oblique views supplemented the above findings.

Fluoroscopically pulsations in the mass synchronous with the aorta were seen in some cases and barium studies of the esophagus showed displacement of the esophagus usually to the left and posteriorly. No esophageal displacement to the right was observed and this, if present, is against a diagnosis of innominate artery aneurysm.

Other studies undertaken in some of the cases included laminagraphic, kymographic and angiocardiographic investigations.

The differential diagnosis must include lesions of a vascular origin and those of a nonvascular nature. The vascular lesions include: (1) aneurysms arising from the aortic arch; (2) congenital aneurysm of the superior vena cava; (3) cavernous hemangioma of the right superior mediastinum; and (4) "buckling" of the innominate artery in arteriosclerotic patients. Angiocardiography usually led to the correct diagnosis in these cases.

The nonvascular group includes: (1) mediastinal metastases; (2) bronchogenic carcinoma; (3) lymphoma; (4) primary neoplasms of the mediastinum such as thymoma, parathyroid tumors, substernal thyroid tumors, neurogenic tumors, lipomas, bone tumors of thoracic cage origin (chondrosarcoma, osteogenic sarcoma), teratomas, dermoid and echinococcus cysts; (5) primary tumors of the right upper lobe of the lung; (6) tuberculomas of the superior mediastinum; and (7) Boeck's sarcoid.—*Donald N. Dysart, M.D.*

Honig, Edward I., Dubilier, William, Jr., and Steinberg, Israel. Significance of the buckled innominate artery. *Ann. Int. Med.*, July, 1953, *39*, 74–80.

The authors found 12 cases of buckling of the innominate artery in 104 angiocardiograms of hypertensive individuals.

The report is made to emphasize the possibility of a right upper mediastinal mass being due to buckling of this artery. They think that angiocardiography is the best way to establish this diagnosis.

If the correct diagnosis is made in these cases, a needless operation can be avoided.—*Frank M. Windrow, M.D.*

Hughes, Frank A. Aneurisma de la arteria renal. Documentacion arteriografica operatoria. (Aneurysm of the renal artery; operative arteriographic documentation.) *Arch. españ. urol.*, April, 1953, *9*, 83–99.

This is a case report of a man, aged forty-two, who complained of right lumbar pain aggravated by riding horseback. A calcific density of semilunar shape was observed on the anteroposterior and oblique roentgenograms to overlie the right renal area. An excretory urogram revealed an extrinsic pressure on the renal pelvis. Pneumopyelography likewise revealed an extrinsic pressure defect. Preoperative arteriography showed an aneurysm of one of the principal branches of the right renal artery. Right nephrectomy was performed.

Review of the literature elicited 115 reported renal aneurysms, occurring mostly between the ages of forty-one and seventy. True aneurysms, containing at least a portion of intact arterial wall, are differentiated from false aneurysms which reveal a ruptured wall. True aneurysms usually result from the degeneration of elastic fibers, although 30 per cent have a history of antecedent trauma. Fifty per cent of patients with false aneurysms gave a history of antecedent trauma.

In some patients true renal aneurysms are associated with hypertension. Other renal aneurysms may be congenital, may be caused by syphilis or periarteritis nodosa, or may be the result of degenerative change.

If the opposite kidney is normal the best treatment is nephrectomy.—*Charles Nice, M.D.*

Gvozdanović, V., Hauptmann, E., Najman, E., and Oberhofer, B. Percutaneous splenic venography. *Acta radiol.*, July, 1953, *40*, 17–26.

Portal hypertension with concomitant varicosities in the esophagus and gastrointestinal tract has a rather unfavorable prognosis. Surgery of the portal hypertension depends on the etiology and the operator should know the site of the disturbance in the circulation.

The authors have used venography by percutaneous injection of 20 cc. ioduron 70 per cent into the spleen in 14 cases, four of which were children. Nine cases were performed by inserting the needle through the lower chest wall into the spleen, while 5 were injected by the transabdominal puncture method. They have now abandoned this latter method. The technique is described in detail.

The indications are splenomegaly of obscure etiology and suspected obstruction in the portal circulation.

There were no serious complications in their cases although they do not consider the procedure to be without its dangers.

Serial roentgenography was done.—*C. Peter Truog, M.D.*

Harvard, Marvin. Renal angiography. *J. Urol.*, July, 1953, *70*, 15–19.

The author reports on his experience with over 100 cases of renal angiography using 75 per cent neoiopax via the translumbar route of injection. The equipment is similar to that of Smith, excepting for the substitution of polyvinyl plastic tubing for the adapter because of the ease of sterilization. The anesthesia and method of injection are similar to those previously described. Satisfactory studies were obtained using the 500 milliampere machine with a high speed Bucky diaphragm and a 0.2 second exposure. Two exposures, one during injection and another immediately after changing the cassette, were routinely made, and it was found that this method was more satisfactory than the use of a rotary cassette changer. The patient usually tolerated more than one injection if the first films were unsatisfactory. Transient mild reactions, usually following injection of the medium directly into a branch of the aorta, were noted, and there were no fatalities. Unsatisfactory angiograms were usually caused by faulty injection technique, mechanical failure of the apparatus, obesity and the wide variation in origin of the aortic branches.

The indications for renal angiography are numerous. It can be used as an adjunct to other renal studies in the determination of the status of one or both kidneys. It is of diagnostic aid in the following: (1) Evaluation of renal blood supply in cases where diminished renal function raises the question of nephrectomy. Demonstration of the presence of at least 50 per cent of the interlobular arteries normal in density and distribution indicates the kidney may be preserved. (2) The differentiation of cortical tumors from cystic disease. A cortical tumor which has undergone cystic degeneration may present a difficult diagnostic problem. (3) The demonstration of various congenital anomalies and the planning of their corrective surgery. (4) The diagnosis and study of upper abdominal masses, essential hypertension, hypertension of doubtful etiology, and chronic pyelonephritis.—*George W. Chamberlin, M.D.*

RADIATION THERAPY

Buschke, F. Vierzehn Jahre Supervolt-Röntgentherapie im Swedish Hospital, Seattle, USA. (Fourteen years of supervoltage roentgen therapy at Swedish Hospital, Seattle, USA.) *Schweiz. med. Wchnschr.*, July 11, 1953, *83*, 641–645.

In 1932 a General Electric supervoltage roentgen therapy apparatus was installed at the Swedish Hospital in Seattle. This apparatus which is operated at 800 kv. (peak) has been in continuous clinical use since then, first under the directorship of Drs. Charles Ward and John Wirth, and since 1938 under the personal supervision of Dr. Cantril and the author. The number of cases treated between 1932 and 1938 was 492, and from 1938 to the present time, 1,224 cases.

Based on an analysis of this wealth of material, the author discusses the clinical usefulness, indications, limitations and various technical procedures of supervoltage roentgen therapy. He also briefly considers the relative value of this form of therapy as compared to surgery and other radiological methods in the treatment of cancer.

As regards the clinical usefulness, it may be said that the fundamental biologic reactions are in the main identical with those produced by ionizing radiations of other qualities, but the mode of irradiation

in certain situations is definitely more efficient, and therefore the clinical results are better.

The author establishes the following indications for supervoltage roentgen therapy: (1) deep-seated tumors arising from organs which cannot be adequately irradiated with deep roentgen rays: bladder, esophagus, trachea, vagina; (2) situations necessitating irradiation through bone: nasal accessory sinuses, epipharynx, hypopharynx; (3) situations in which it is desirable to administer the full dose through one single field: oral mucosa, base of the tongue, salivary glands; (4) situations requiring a combination of local surgery or radiologic procedures with massive roentgen irradiation: tongue, oral mucosa (larynx, esophagus); (5) cases in which previous inadequate irradiation failed to destroy the cancer. A detailed account is given of the results obtained in these various situations by paying particular attention in the several techniques employed.

A limitation of supervoltage roentgen therapy is that, in contradistinction to deep roentgen therapy, the reaction produced on the skin or mucosa cannot be used as a biologic index of the permissible dose to be given. Unawareness of this fact in the early days resulted not infrequently in irreparable late injury to some of the deeper structures, as for example, gastrointestinal tract, vascular connective tissue, bone, etc., occasionally leading to death or permanent disability of the patient. It is important, therefore, that the magnitude of the dose to be administered in a particular instance be determined on the basis of tolerance of the deep-seated tissues rather than on the clinical observation of the cutaneous or mucosal reaction. The author stresses that with the present trend of using very high voltages a careful analysis of this relationship of the depth dose to the surface dose is imperative to avoid even more catastrophic damages in the future.

In comparing the relative value of supervoltage roentgen therapy with that of surgery or deep roentgen therapy, the author concludes that in about 10 per cent of the cancer cases, in which the other procedures would usually fail, supervoltage roentgen therapy produces a definite cure. In most of the remaining cases it permits treatment of the cancer with less damage to the skin and a lesser general reaction of the patient than is possible with deep roentgen therapy. For this reason it can safely be predicted that supervoltage roentgen therapy will form a permanent part of our future cancer treatment armamentarium.—*T. Leucutia, M.D.*

Foltz, Eldon L., Holyoke, John B., and Heyl, Henry L. Brain necrosis following x-ray therapy. *J. Neurosurg.*, July, 1953, *10*, 423–429.

A forty-five year old white woman was treated on the right temporal scalp for a basal cell epithelioma with 2,500 r (air) of unfiltered 120 kv. roentgen rays to an area 5 by 5 cm. Two and a half years later the tumor recurred and was excised. Shortly thereafter the patient developed symptoms of an expanding intracranial lesion, and was found at surgery to have a nontumorous mass approximately 4 cm. in diameter in the right parietotemporal cortex directly underlying the irradiated skin. Pathologic study showed the lesion to be an ischemic infarction of the brain caused by progressive, obliterative, vascular disease as manifested by (1) hyalinization and thickening of the blood vessel walls, with resulting luminal narrowing, (2) suggestive amyloid degeneration, and (3) telangiectasis of the subpial vessels. The blood vessels in the brain immediately adjoining the necrotic lesion were normal.

The radiation vascular damage cannot logically be explained by the simple interpretation of overdosage. Rather, the authors feel that certain obscure abnormalities of the specific cerebrovascular system under treatment must be involved.—*Arthur S. Tucker, M.D.*

Laborde, Simone, and Montagnon, Jean. Emploi des méthodes radiologiques dans le traitement des cancers du corps utérin. (Use of radiologic methods in the treatment of cancer of the corpus uteri.) *J. de radiol. et d'électrol. & Arch. d'électric. méd.*, 1953, *34*, 479–483.

The accepted treatment for cancer of the corpus uteri in France is exclusively surgical for two reasons: (1) it is claimed that the results obtained by this method are excellent, and (2) it is assumed that since the adenocarcinomas are radioresistant, radiologic methods would be of no value.

The authors took exception to this established practice and since 1948 they have treated 32 cases of carcinoma of the corpus uteri with intracavitary radium. In the present article, they describe in detail the technique used by paying considerable attention to hysterography which they consider indispensable for localizing the site of the lesion before treatment and for evaluating the response to irradiation in the follow-up period.

Briefly, the technique is as follows: Multiple radium tubes of 10 mg. each, filtered with 1.5 mm. Pt, are used by following the "packing method" of Heyman introduced in 1932. However, to obtain a better conformation to the shape of the usually enlarged uterine cavity, three to four radium tubes are placed in tandem within a soft rubber catheter of 8 to 11 cm. length and three to four such catheters are introduced into the uterine cavity. An additional 10 mg. radium tube is placed in the cervical canal. If the uterine cavity is not enlarged, the 10 mg. radium tubes are inserted one by one until the cavity is filled. Thus the series of treatments consists of 70 to 120 mg. radium element applied for three days, corresponding to 5,000 to 8,600 mg. hr. The entire

series is repeated in three to four weeks, preferably three weeks. The authors do not use complemental roentgen therapy.

The hysterography is performed under fluoroscopic control, by using the water-soluble diodone as contrast medium. This substance diffuses readily and thus permits a more accurate visualization of the shape and size of the carcinoma. It also aids in performing a "guided" biopsy instead of the blind curettage, thus eliminating possible confusion with a carcinoma of the cervical canal. Several samples of beautiful hysterograms made before and at various intervals after completion of the treatment are included.

The results obtained in the 32 cases are analyzed.

In concluding, the authors express the opinion that the exclusively surgical treatment of carcinoma of the corpus uteri should be replaced by a method consisting of preoperative radium therapy and hysterectomy. Even in the inoperable cases, intrauterine radium application leads to marked palliation and not infrequently to long survival of the patients.—*T. Leucutia, M.D.*

RADIOISOTOPES

Coliez, R., Tubiana, M., Dutriex, J., and Guelfi, J. Résultats du traitement de 43 cas de cancer du corps thyroïde par l'iode radio-actif. (Results of treatment of 43 cases of cancer of the thyroid gland with radioactive iodine.) *J. de radiol. et d'électrol. & Arch. d'électric. méd.*, 1953, *34*, 305–321.

The authors treated with radioactive iodine 43 cases of cancer of the thyroid gland which were selected on the basis of I^{131} tracer study from a total of 140 cases. In the present article they describe (1) the general technique of treatment, (2) the various test performed during the course of treatment, (3) the clinical findings during the course of treatment, (4) the effects of treatment and (5) the statistical results.

All of the 43 cases are reported in a tabular form by listing the sex, age, duration, histologic findings, status and stage of the disease prior to treatment, individual and total dosage and the final outcome in each case.

The authors emphasize in particular the difficulties of selecting the patient suitable for I^{131} therapy and of properly calculating the required dosage. They state that to obtain a worthwhile result, a dose of at least 500 rep must be administered to the tumor area by avoiding at the same time a dose larger than 300 rep to the very sensitive tissues, especially of the hemopoietic system. A preliminary I^{131} tracer study is essential to determine the mode of uptake of the radioactive iodine by the primary cancer of the thyroid gland as well as by the metastatic lesions and thus adequately adjust the dose to the necessary indications.

The following are the results obtained: (a) of 13 patients with inoperable local cancer either because of the large size of the primary tumor or the poor general condition, 6 survived for periods varying between five months and two years and nine months; (b) of 6 patients with active functioning metastases, 4 survived for periods of from thirteen months to two years and eight months; (c) of 11 patients with incompletely removed or recurrent local cancer, 8 are in excellent general condition and of these 5 survived for more than two years; (d) one single patient was treated with I^{131} preoperatively and he died four days after the surgical intervention; (e) of 12 patients with advanced metastases and poor general condition, 5 died within two months, 6 died within an interval of from four to eight months and only 1 patient is alive after seven months.

The authors conclude by mentioning that in several of their cases the metastatic lesions acquired during the course of the treatment a significant avidity for the radioactive iodine whereas no uptake was demonstrable at the first preliminary test.—*T. Leucutia, M.D.*

Bradley, Walter O. Radioactive iodine as an indicator of the uptake of iodine by the liver, gastrocnemius, and thyroid of *Rana pipiens*. *Science*, May 1, 1953, *117*, 483–484.

Male and female frogs were given intraperitoneal injections of 22.5 mc. of carrier-free radioactive iodine in a sodium bisulfite solution.

Sacrifice four hours later and study with a Geiger-Müller counter showed that slices of thyroid tissue displayed the greatest radioactivity, followed by liver and striated muscle in decreasing order. The results paralleled those obtained by others in rats and sheep.—*T. J. Wachowski, M.D.*

Walter, J. Radioactive gold in malignant effusions. *Proc. Roy Soc. Med.*, June, 1953, *46*, 466–471.

The author reports eighteen months' experience using colloidal radioactive gold to control malignant effusions of the chest and abdomen.

Usually a preliminary tap is done to remove most of the fluid. Then, under suitable precautions, the Au^{198} is injected as a volume of 100–150 ml. Recently, more concentrated solutions have been used. The wound is sealed with collodion and the patient rotated to various positions for two hours, to help obtain uniform distribution of the solution. This is checked by surveying the patient with a Geiger counter. The author had no difficulty in obtaining uniform distribution.

The amount injected ranged from 140–250 mc. He now uses 170 mc. routinely. The radiation reactions have been mild. Fifteen abdominal cases were

treated and 7 had some measure of benefit. Of 4 thoracic cases, all treated bilaterally, 1 received some relief.

Several of the cases were terminal at the time of treatment and at postmortem showed marked thickening of the serosal surfaces. Measurements of the radioactivity remaining in several of the organs were made and tissue doses calculated.—*George L. Sackett, Jr., M.D.*

Goldblith, Samuel A., Proctor, Bernard E., Davison, Sol, Lang, David A., Kan, Billy, Bates, Charles J., and Karel, Marcus. Studies on the dosimetry and bactericidal effects of gamma radiations from a cobalt^{60} source. *Radiology*, May, 1953, *60*, 732–736.

As part of the studies, begun in 1943, of the effects upon microorganisms of ionizing radiations produced by particle accelerators, the Department of Food Technology at the Massachusetts Institute of Technology has undertaken investigation of the effects obtained from radioactive cobalt 60. One kilocurie of cobalt 60 was used as a source. Dosimetry factors and techniques are discussed, and the relative radiosensitivities of 11 bacterial species to the gamma rays of cobalt 60 are presented. Relative sterility dose requirements have been noted experimentally and by calculation, and the results were found to be substantially alike.

The authors make it clear that radiologic processing of foods is not yet practical, and that further studies are necessary. The variability of sensitivity of various pathogens, and the acceptance of allowable numbers remaining viable, constitute two important problems.—*Lynne J. Taylor, M.D.*

Arden, G. P., and Veall, N. The use of radioactive phosphorus in early detection of avascular necrosis in the femoral head in fractured neck of femur. *Proc. Roy. Soc. Med.*, May, 1953, *46*, 344–346.

Avascular necrosis in the femoral head occurs in about 30 to 40 per cent of the cases of the fractures of the neck of the femur treated by nailing. Radioactive phosphorus gives a new method of investigating the blood supply of the femoral head.

A dose of 1 to 2 cc. of P^{32} is given intravenously one hour before the nailing operation. At operation two samples of bone are removed, one from the trochanteric region as a control and the other from the head of the femur. These are dried and weighed and their radioactive content measured.

More recently the technique has been modified to give direct readings at the time of operation by means of a needle counter inserted into the head of the femur and connected with a clinical monitor. By this means it is possible to decide at the time of operation whether the blood supply to the femoral head is damaged or not.—*Leslie K. Sycamore, M.D.*

Kohl, Douglas A. A multiple-counter system for isotope encephalometry. *Nucleonics*, July, 1953, *11*, 16–19.

A multiple-detector positioner is described holding eighteen individual shielded Geiger-Müller tubes arranged symmetrically over the skull. The axes of the tubes converge at a common central point and each tube is attached to an individual amplifier and scaler to provide maximum flexibility. Gang-switched circuits permit accurate survey and analysis in twenty-five minutes. Greater accuracy is claimed for this system over a simpler method using a single Geiger-Müller tube with a marked cap as a positioning device. Further refinements in analysis of the data thus obtained are also described.

The application of this method is reported in 42 patients. Thirteen out of 17 tumor patients were correctly judged; 17 out of the remaining 25 patients were called normal. Further diagnostic evaluation is promised in future publications.—*J. Maurice Swain, M.D.*

Bakay, Louis. Studies on blood-brain barrier with radioactive phosphorus. III. Embryonic development of the barrier. *A.M.A. Arch. Neurol. & Psychiat.*, July, 1953, *70*, 30–39.

In order to determine whether or not a blood-brain barrier exists at birth, P^{32} was given to 9 adult rabbits, 5 of them being pregnant, and 4 used as controls. Four of the pregnant rabbits were sacrificed at various periods of gestation, the other saved for study of the radioactive offspring.

Findings by measurement of radioactivity of dried tissue and blood samples and in a few cases by radioautographs showed higher and more generalized uptake by the embryonic and fetal tissues than by adult tissues. The blood-tissue ratio drops shortly before term, only to rise again slightly in the newborn rabbit. Cerebral level of P^{32} is high for the few postnatal weeks and then drops to adult level.

Absolute liver values show little variation with age and this was found to be true in other organs also.

The author presents a review of the literature on placental permeability and cerebrovascular permeability and describes a case of P^{32} transfer, the tracer given eighty hours prior to delivery of a macerated human five month fetus. He concludes that there is no single specific answer to the problem of a blood-brain barrier and that its existence is dependent on capillary development and metabolic requirements.—*Robert W. Emerick, M.D.*

Corrigan, K. E., and Hayden, H. S. Failures, flops and false localizations in tracer technic. *Radiology*, June, 1953, *60*, 870–884.

Tracer technique is an exceptionally valuable means of diagnosis. When used carefully in cooperation with other methods, its capabilities are almost unlimited. So that its potentialities and its limitations may be better appreciated, the authors discuss pitfalls, inaccuracies and difficulties they encountered in their clinical isotope program.

A total of 2,711 tracer studies were conducted on 2,367 patients. There were 13 failures and false localizations. The most serious of these were 3 carcinomas of the thyroid which were missed and 3 cases which were believed to be carcinoma of the thyroid that later could not be proved. A total of 119 cases of carcinoma of the thyroid were identified correctly by tracer technique.

Twenty-eight diagnostic problem cases, which proved to be thyroiditis, were encountered. Abscess formation had occurred in some of these cases. An active thyroiditis is characterized by the fact that foci of hyperactivity outline the acute area. Portions of the gland which had been damaged by the inflammatory process appear to be completely without function.

The authors state that the identification of mediastinal shadows and the localization of toxic retrosternal thyroids are usually very simple. It is their standard procedure to administer 100 microcuries of radioactive phosphorus (P^{32}) when a radioiodine tracer on a mediastinal mass is negative. The radioiodine will clear from the blood stream within forty-eight hours and thereafter, if the mediastinal shadow is due to an actively growing tumor, a good concentration of P^{32} can be found. Some tumors, particularly those of the lymphoma group, have such an extremely rapid rate of concentration of this isotope that their tracer pattern is almost specific.

Diagnostic problem cases and undesirable incidents are considered in detail. Factors conducive to error are discussed, and suggestions are given to permit accurate diagnosis in the difficult and complicated case.—*Arno W. Sommer, M.D.*

Goodwin, William E., Cassen, Benedict, and Bauer, Franz K. Thyroid gland weight determination from thyroid scintigrams with postmortem verification. *Radiology*, July, 1953, *61*, 88–92.

In the calculation of a single therapeutic dose of I^{131}, several factors have to be taken into account: (a) The estimated amount of radiation to be delivered to the gland, (b) the maximum uptake of administered I^{131} by the gland, (c) the effective half-life, and (d) the weight of the gland. Until very recently the thyroid gland weight had to be estimated by palpation. This made accurate calculation of a therapeutic dose of I^{131} extremely difficult.

A more accurate method, recently described by Allen and Goodwin, was used by the authors. Using a "scintiscanner," actual size scintigrams of the gland were obtained, after administration of about 250 microcuries of I^{131}. Estimate of thyroid gland weight was determined by applying the formula as developed by Allen and Goodwin. The weight of the gland in grams is equal to 0.32 × the area of the scintigram in square centimeters × the maximum length of the lobe in centimeters.

The weight of the thyroid glands of 4 patients was calculated from thyroid scintigrams by this method. Three of these patients subsequently died of heart disease and one underwent thyroidectomy. The actual weight of these specimens agreed well with the weight determined from thyroid scintigrams.—*Arno W. Sommer, M.D.*

Baumeister, Carl F. Radioiodine tracer and biopsy in the diagnosis and treatment of hyperthyroidism. *A.M.A. Arch. Surg.*, July, 1953, *67*, 80–91.

The author discusses the unreliability of any single test in evaluating thyroid function and especially in using it for the diagnosis of hyperthyroidism. He feels that for practical clinical purposes, correlation of the basal metabolic rate, radioiodine tracer studies and thyroid biopsy with the clinical picture will give the best evaluation of the thyroid state.

Four interesting cases felt to be hyperthyroidism are reported to illustrate the pitfalls of relying upon any single test or upon the clinical picture. Only one turned out to have hyperthyroidism. If all the of findings had been properly correlated, a reasonably good evaluation of the patient from a practical clinical standpoint would have been obtained.—*Norman Heilbrun, M.D.*

Larsson, Lars-Gunnar, and Ragnhult, Inger. A study of the iodine-concentrating function of the thyroid after treatment with radioactive iodine. *Acta radiol.*, June, 1953, *39*, 477–484.

Despite the difficulty in accurately establishing a proper thyroid irradiation dose of I^{131} due to variations in concentration and uptake of the isotope in the gland and variations in thyroid volume, good results have been obtained with the "single dose" technique. It is pointed out that this probably is due to a good therapeutic margin between subtotal and total thyroid destruction, but the possibility of thyroid regeneration may also be an important factor and forms the basis of this investigation.

Twenty-three thyrotoxic patients and 10 euthyroid cardiac patients were treated with varying doses of I^{131}. The thyrotoxic patients received from 3 to 15 millicuries, depending on estimated size of the gland. Euthyroid patients received 6 to 8 mc. Tracer studies were done before and after treatment and these consisted of a single twenty-four hour uptake and excretion estimation. Check-up tracers were

done three months, six months and, in a few instances, eight to ten months after treatment.

Of the 23 thyrotoxic patients, 3 developed and maintained a very low thyroid uptake of I^{131} and clinically had myxedema. The other patients showed depression in uptake two to four months after treatment. Uptake increased in five to eight months but was usually below the level prior to treatment.

Of the euthyroid group with severe cardiac failure, 3 patients constantly had a very low I^{131} uptake and clinically were hypothyroid. The other 7 patients showed a depression in uptake at two to four months and a relative increase in uptake after five to nine months. The degree of depression in uptake on the final tracer was not as great as in the thyrotoxic group.

The authors believe that radioiodine treatment is followed by depression of the iodine concentrating capacity of the thyroid which reaches its minimum within three months. Regeneration of function occurred in most cases after five to nine months. Six months after treatment the functional level has become stable. These findings are of obvious importance in radioiodine treatment and evaluation of results of therapy.—*Robert W. Emerick, M.D.*

Storaasli, J. P., Bone, F. J., King, D. P., and Friedell, H. L. The use of radioactive colloidal gold in the treatment of serous effusions of neoplastic origin. *Surg., Gynec. & Obst.*, June, 1953, *96*, 707–710.

Intracavitary radioactive colloidal gold was first used for the treatment of peritoneal and pleural effusions due to carcinomatosis by Mueller in 1950. He showed that the introduction of this substance impeded the formation of serous effusions. Since the number of cases thus far reported is small and since this form of treatment appears to be a valuable contribution to the palliative management of the patient with widespread carcinoma, the authors are presenting their results in 19 patients.

Characteristics of Au^{198}. Radioactive gold emits a beta particle of 0.98 mev. peak and 2 gamma photons. Its half-life is 2.7 days so that it delivers approximately 75 per cent of its radiation in 5.5 days. When given intravenously it is deposited mainly in the reticuloendothelial system of the liver. When introduced into a serous cavity, it is deposited over the serous surface.

Technique of Treatment. In the treatment of ascites due to peritoneal carcinomatosis, a paracentesis is done and 75 to 125 millicuries of the radioactive colloidal gold are introduced into the peritoneal cavity. For intrapleural administration of the gold, it is introduced through a thoracentesis needle and a dose of 35 to 75 millicuries is used.

Summary. Thirteen of the authors' patients were treated for ascites and 6 for pleural effusion of neoplastic origin. Beneficial results were obtained in approximately two-thirds of the patients. Effusion due to metastases from carcinoma of the ovary appeared to respond most favorably.

The authors believe that treatment with radioactive colloidal gold is a valuable adjunct to other forms of therapy in the palliative management of such patients.

There is no evidence that this treatment prolongs life.—*Mary Frances Vastine, M.D*

Lushbaugh, C. C., Storer, J. B., and Hale, D. B. Experimental acute radiodermatitis following beta irradiation. I. Its pathogenesis and repair. *Cancer*, July, 1953, *6*, 671–677.

Using Sr^{90} as a beta source, 14,000 rep, delivered at the rate of 90 rep per second, was given to the shaved abdomens of 216 Sprague-Dawley rats. The animals were sacrificed every other day for thirty-six days, and a detailed study of the morphological changes occurring in the production and repair of ulcerative radiodermatitis was made.

A latent period of four days in which no changes were noted was followed by a progressive degeneration and necrosis of the epithelium and corium in the six day period. Regeneration of the epithelium and fibroplasia in the deep portion of the skin occurred between fifteen to twenty days, and by the thirty-sixth day there was complete healing.

The authors attribute the difference between the healing of ulcerations caused by beta rays and those caused by other types of more deeply penetrating ionizing radiations to the presence of healthy cicatrization occurring in the deeper portions of the beta-irradiated skin which pushed the injured but still viable structures of the middle and deeper portions of the dermis to the surface so that the defect can be filled.—*John P. Storaasli, M.D.*

Lushbaugh, C. C., and Storer, J. B. Experimental acute radiodermatitis following beta irradiation. II. The inhibition of fibroplasia. *Cancer*, July, 1953, *6*, 678–682.

The slow and protracted healing of acute and ulcerative radiodermatitis has been attributed in part to the inhibition of fibroplasia by irradiation. Using surgical incisions as a stimulus to fibroplasia, studies of fibroblastic activity in the normal and irradiated skin of rats were carried out. The irradiated skin was exposed to 10,000 or 28,000 rep of beta radiation either before or after the surgical incision.

Morphological studies in those animals in which the surgical incision was made after irradiation showed that while normal cellular exudate developed promptly, fibroblasts failed to appear and proliferate in the irradiated area. If the surgical incision was made before the area was irradiated, the fibroblasts that began to proliferate were arrested and underwent changes that resulted in the formation of giant anomalous forms. The study further showed that the

amount of fibroblastic activity was inversely proportional to the amount of irradiation.—*John P. Storaasli, M.D.*

Lushbaugh, C. C., and Hale, D. B. Experimental acute radiodermatitis following beta irradiation. III. The changes in water, fat, and protein content. *Cancer*, July, 1953, *6*, 683–685.

Changes in water, fat and protein content of skin and subcutaneous tissue of rats given 28,000 rep of beta radiation from P^{32} were studied. The animals were sacrificed and samples were taken of normal and irradiated skin at frequent intervals up to sixteen days following irradiation. The increase in water and decrease in fat and protein content described as being typical of normal skin healing was delayed and did not reach a maximum in the irradiated skin until the thirteenth day after exposure. These observations compared well with the slow development of morphological changes previously reported.—*John P. Storaasli, M.D.*

Lushbaugh, C. C., and Hale, D. B. Experimental acute radiodermatitis following beta irradiation. IV. Changes in respiration and glycolysis. *Cancer*, July, 1953, *6*, 686–689.

A comparison of tissue repsiration and glycolysis was made between normal skin and that given 14,000 or 28,000 beta rep with Sr^{90}. Following an early (2 hr.) slight depression of respiration and glycolysis in irradiated skin, a marked increase in the glycolytic rate was observed at twenty-four and forty-eight hours. This was followed by a decline to normal in four to six days, with a subsequent depression to subnormal levels when necrosis of the tissue was observed. The early stimulation of glycolysis preceded any microscopic sign of injury. The authors suggest that the most logical explanation of this stimulating effect is an early destruction of enzymes, such as sulfhydryl enzymes, or substances necessary for the control of the rate of metabolic activity.

It is interesting to note that even doses near 1,000,000 rep failed to completely inhibit glycolitic activity of skin immediately.—*John P. Storaasli, M.D.*

Lushbaugh, C. C., and Hale, D. B. Experimental acute radiodermatitis following beta irradiation. V. Histopathological study of the mode of action of therapy with Aloe vera. *Cancer*, July, 1953, *6*, 690–698.

For many years extracts of the leaves of the *Aloe vera* plant have been used efficaciously in the treatment of acute and chronic radiodermatitis.

The authors, in a carefully controlled study using the irradiated skin of rabbits, have shown rather impressively that *Aloe vera* promotes more rapid healing. Rabbits were irradiated locally on the back with 14,000 and 28,000 rep and these areas were either left untreated, treated with fresh whole leaf of *Aloe vera*, or treated with a commercially available ointment made from *Aloe vera*. The gross and morphological changes were then compared. It was found that treatment with *Aloe vera* hastened both the degenerative and reparative phases of the lesion so that an ulcer which would not heal in four months without treatment, healed completely in two months.—*John P. Storaasli, M.D.*

Brown, J. G. Observations of the scattered radiation inside and outside a 1,000-curie cobalt^{60} teletherapy room. *Radiology*, July, 1953, *61*, 82–87.

The results of a radiation survey around a large Co^{60} teletherapy unit are given. Temporary $8\frac{1}{2}$ inch walls of solid concrete blocks and a 6 foot thick "back stop" of sandbags on an outside wall behind the patient were tested. They were found to give inadequate protection if an eight hour day under the most hazardous techniques of operation and constant habitation were the rule. However, under normal circumstances of 4.5 hours exposure per day and vertical placement of the beam through the basement floor three-fourths of the time, this economical system maintains scattered radiation generally within safe limits of 6.25 milliroentgens per hour.

It was found necessary to add a $\frac{1}{8}$ inch lead shield on the wall by the technician's desk. Ceiling protection of 4 inches of concrete and $\frac{1}{4}$ inch lead gave good protection and scattered radiation was detected only when the beam was directed horizontally toward the "back stop" wall.

The amount of scatter was directly proportional to the field size. Doubling the lateral dimension of the water phantom decreased the nearby scatter by 15 per cent. Increasing the dose rate increased the amount of scatter more or less proportionately. The half-value layer of scattered radiation is greater with 45° than 90° incident scatter because of its greater distance of travel through the concrete wall.

It was demonstrated to be advantageous to have the entrance door situated in an offset maze arrangement. This allows the use of only $\frac{1}{8}$ inch lead additional protection and circumvents the need for a massive lead door with an elaborate mechanical system for operation.—*William A. Goodrich, Jr., M.D.*

Gomberg, H. J., and Gould, S. E. Effect of irradiation with cobalt-60 on trichina larvae. *Science*, July 17, 1953, *118*, 75–77.

The authors describe in detail the effects of irradiation with different doses on both isolated and encysted trichina and trichinous rat muscle. The radiation source employed was cobalt-60 and the study was undertaken to compare the effect of cobalt-60

and 200 kv. radiation. The different doses determined for death, inhibition of maturation, and sexual sterilization of larvae are presented graphically. Statistical studies show that 18,000 r is sufficient to inhibit 100 per cent maturation and that 15,000 r produces complete sterilization of the mature female of the trichina.

All of these studies were made on rats. The authors feel that irradiation of pork as a method of controlling trichinosis is a possibility. Undesirable flavor changes have been noted in numerous foods which have been treated with preserving doses of radiation up to about 2,000,000 r. They feel, however, that 1/100 of that dose is adequate to prevent maturation of trichinae. Furthermore, tests of pork irradiated with doses up to 38,400 r have shown no appreciable flavor changes. A further report is to be published.—*P. B. Parsons, M.D.*

CHEMOTHERAPY

Werner, K. Die Behandlung des Röntgenkaters mit Dihydroergotamin. (The treatment of roentgen sickness with dihydroergotamine.) *Schweiz. med. Wchnschr.*, May 2, 1953, *83*, 431–432.

The multiplicity of medications recommended for the treatment of roentgen sickness seems to be proof that no drug is entirely satisfactory. The biological effect of radiation is so complicated and so little understood that none of the many theories explains the symptoms nor offers a definite means of their relief.

After trying out many different types of medications with unsatisfactory results the author used dihydroergotamine. Of 1,515 patients who received roentgen therapy 19.7 per cent suffered from roentgen sickness to some degree. The drug (1 cc. of the solution contained 2 mg.) was given in doses of 10 to 20 drops three times a day. Two hundred and ten patients with roentgen sickness were treated in this fashion. They were benefited considerably more than 132 others who were treated either by sedation or belladonna or vitamin B complex. Practically no side effects due to the drug were noted.—*Hans W. Hefke, M.D.*

Hultberg, Sven. Local enzymatic treatment of radiation necroses of the skin. *Acta radiol.*, April, 1953, *39*, 343–352.

Varidase, a mixture of the enzymes streptokinase and streptodornase, made by Lederle Laboratories, has according to many publications been used in the treatment of certain infections and other diseases. The author stresses the value of this compound as an adjunct to the therapy of necrotic radiation ulcers, and reports the results in 15 cases. In all of these there was rapid cleansing of the necrotic area and accelerated healing.

Treatment Technique. In treating necrotic radiation ulcers, the author usually started with a rather concentrated solution of varidase, using 10 cc. of isotonic sodium chloride as a solvent for the desiccated substance in one vial. After two or three days, a more dilute solution using 20 cc. instead of 10 cc. was employed.

Sterile cotton gauze, soaked in the varidase solution, was applied to the wound and this was covered with cellophane or plastic sealed to the skin. The gauze was changed 3-4 times a day and the treatment was continued from three days to a week.

Supplementary antibiotic therapy proved of great value in some patients.

In 2 cases in which the necrotic ulcers were largely covered by fibrous tissue, the effect of the varidase treatment was at first rather poor, but when the scraps were removed mechanically, the varidase produced a prompt result.—*Mary Frances Vastine, M.D.*

Criep, Leo. H., and de Castilho Ribeiro, Creso. Allergy to procaine hydrochloride with three fatalities. *J.A.M.A.*, April 4, 1953, *151*, 1185–1187.

The authors report 3 fatalities, encountered in one year, resulting from an immediate reaction to procaine hydrochloride. Though a very large number of patients receive this drug daily without reaction, on rare occasions serious unexpected side effects may occur. In the first patient, an asthmatic, death followed the introduction of 1 per cent procaine hydrochloride preliminary to bronchography. A roentgenogram taken just before death when a small amount of opaque oil had been introduced showed that it was distributed in the trachea and main bronchi. This was interpreted as evidence for obstruction due to bronchospasm in the smaller bronchi. In the second case, the patient died following an intercostal nerve block with 2 per cent procaine hydrochloride. The patient had received this drug on many occasions previously and had undergone major surgery on two occasions. The third patient, a woman aged twenty-nine, died following the administration of procaine hydrochloride for routine dental extraction.

The authors suggest that skin tests are of no diagnostic value but that intranasal application, or sublingual, or intraconjunctival administration of a small amount of the drug may indicate sensitivity.—*Lawrence A. Davis, M.D.*

Barnes, Allan C. The production of ACTH in the patient undergoing gynecologic surgery or receiving pelvic irradiation. *Am. J. Obst. & Gynec.*, April, 1953, *65*, 758–772.

This article describes a series of experiments to test the ACTH production in a group of 12 patients, as indicated by the sodium, potassium and nitrogen levels, as well as daily 17-ketosteroid levels, eosino-

phil and lymphocyte counts. One group of patients received pelvic surgery, and the other, pelvic irradiation.

The surgical procedures had a pituitary stimulating effect, the duration being roughly proportional to the extensiveness of the surgery.

The patients receiving irradiation had no response indicative of an alarm reaction, except that related to the insertion of the radioactive needles.

In therapeutic ranges irradiation does not cause a rise in ACTH production.—*George L. Sackett, Jr., M.D.*

Shields, W. E., Adamson, N. E., Jr., and MacGregor, J. B. Peptic ulcer perforation following administration of phenylbutazone. *J.A.M.A.*, May 2, 1953, *152*, 28–30.

Phenylbutazone is being rather widely used for arthritic and rheumatoid conditions. From 23 to 44 per cent of the patients develop some undesirable side-effects. The authors report on 3 cases: one, a perforated duodenal ulcer; another, a perforated gastric ulcer; and the third, a bleeding from a duodenal ulcer following the administration of phenylbutazone.

Case 1: A fifty-four year old white male was given phenylbutazone 400 mg. per day orally for seven days then 600 mg. per day for nine days at which time the perforation of the duodenal ulcer occurred. The patient had no history of gastric distress until the administration of the higher dose of phenylbutazone. The postoperative course was uneventful.

Case 2: A fifty-six year old white female was given 600 mg. of phenylbutazone per day orally for seven days. This medication was stopped and substituted by cortisone given orally, the dose being 250 mg. over a period of forty-eight hours, at which time the patient developed rupture of the prepyloric ulcer. The postoperative course was uneventful.

Case 3: A sixty-one year old white male, who was admitted with a chief complaint of tarry stools, had received phenylbutazone for three weeks at a rate of 300 mg. per day orally. Roentgen examination revealed a duodenal ulcer. The phenylbutazone was discontinued and the melena cleared immediately. The patient was treated for his ulcer and six weeks later the ulcer had completely healed.—*Neal F. Yeomans, M.D.*

Raffensperger, Edward C. Multiple gastric ulcers occurring during phenylbutazone therapy. *J.A.M.A.*, May 2, 1953, *152*, 30–31.

A case is reported with multiple gastric ulcers following phenylbutazone therapy which healed under treatment.

The case is that of a seventy year old white female who complained of epigastric distress which appeared approximately three days after discontinuing phenylbutazone. She had received a total of approximately 20 tablets (200 mg. each) over a two week period. Roentgen examination demonstrated an ulcer on the lesser curvature of the stomach and another somewhat higher on the anterolateral wall of the upper third of the stomach. Checkup examination after two weeks of therapy demonstrated complete healing of the anterolateral ulcer and regression of the lesser curvature ulcer to about one-fourth its former size. Therapy was continued and additional roentgen examination three weeks later demonstrated complete healing of the ulcer.

The author comments on the onset of these two ulcers shortly after a course of phenylbutazone occurring high in the stomach and which healed promptly on institution of proper therapy.—*Neal F. Yeomans, M.D.*

Krainin, Philip. Gastric ulcer with massive hemorrhage following use of phenylbutazone. *J.A.M.A.*, May 2, 1953, *152*, 31–32.

This is a case report of a seventy-two year old white female with osteoarthritis of the spine, shoulders and knees of five years' duration, who was given phenylbutazone 800 mg. daily per os for a week and then 400 mg. daily for about three weeks. At the end of this time she was found in her home in shock.

The family stated that twice that day she had fainted after passing a large quantity of black stool and vomiting some dark red liquid. She was given blood transfusions and other therapy for her shock and ten days later a gastrointestinal roentgen examination was done and a small ulcer crater demonstrated on the lesser curvature of the pars media of the stomach. She was continued on ulcer therapy and five weeks later a repeat gastrointestinal study showed a complete healing of the ulcer.

It has been proposed that patients receive antacids along with phenylbutazone therapy. The author feels that a patient with known peptic ulcer should not be given phenylbutazone. The mechanism by which phenylbutazone produces ulcers is not known. Local irritation has been suggested because of the nausea and vomiting sometimes accompanying oral administration of the drug; however, ulcers have also been reported following the intramuscular injection of phenylbutazone.—*Neal F. Yeomans, M.D.*

Bacq, Z. M., Dechamps, G., Fischer, P., Herve, A., Le Bihan, H., Lecomte, J., Pirotte, M., and Rayet, P. Protection against x-rays and therapy of radiation sickness with β-mercaptoethylamine. *Science*, June 5, 1953, *117*, 633–636.

The authors investigated the protective action against roentgen rays in animals and found many promising substances in the amine group. Of these, cysteamine ($HS—CH_2—CH_2—NH_2$) which is also known under the names of β-mercaptoethylamine,

1573 L and becaptan R. N. proved to have a definite practical value.

Experiments in mice have shown that if a dose of 3 mg. of cysteamine (base, neutralized with HCl to pH 6.5) is injected intraperitoneally one to three minutes before irradiation with 700 r, a permanent survival of 97 per cent is obtained and that the same amount helps raise the lethal dose from 700 r to 1,300 r. However, if the cysteamine is injected 0.5 to three minutes after the end of irradiation, no protective action is observed.

Herve and Bacq reported the favorable effect of cysteamine or β-mercaptoethylamine in the treatment of radiation sickness in humans (see former abstract in this Journal). Many observations from Liège and the various cancer centers in Belgium have confirmed this report. Usually, a single intravenous injection of 200 mg. cysteamine (base, neutralized by enough HCl to obtain pH 6–7) is sufficient to relieve the symptoms of radiation sickness within twenty-four hours; rarely, 2 or 3 injections may be necessary.

The authors attempt an explanation of the apparently contradictory observations in the mice where the injection of the cysteamine after the end of irradiation had no protective effect and the human where such good results are being reported. They are inclined to accept the interpretation given by Cronkite, Brecher, and Chapman for the protective action of glutathione but believe that the physicochemical basis (competition for free radicals) must be expanded by also taking into consideration the relationship of the cysteamine metabolism and the reactions of the body to that substance. Many facts seem to indicate that the liver is the site of important reactions to both the cysteamine and ionizing radiations. Consequently, the cysteamine remains active when given after irradiation only if the liver has been protected as is the case in patients with radiation sickness who usually receive local irradiation, whereas in mice the irradiation is general.—*T. Leucutia, M.D.*

MISCELLANEOUS

Fusi, Giorgio. Saggio sperimentale sulle prime manifestazioni radiologiche di osteoporosi. (Experimental investigation on the first radiologic manifestations of osteoporosis.) *Radiol. clin.*, March, 1953, *22*, 123–129.

The author performed a series of experiments to assay quantitatively the degree of osseous calcium absorption which would produce the first roentgenographically demonstrable changes of osteoporosis.

Whole and sliced normal lumbar vertebrae which were deprived of their appendages but not macerated were immersed into a nitric acid solution of 0.5 per cent strength and then (after a loss of 8.1 per cent of the initial calcium content) into a solution of 5 per cent strength. The decalcifying fluid was subjected to quantitative chemical analysis for calcium everytime the vertebrae were roentgenographed. The exposures of the isolated vertebrae were made in anteroposterior projection first at one quarter hour and later at gradually spaced intervals, by always using the same technique. An aluminum strip with steps of increasing thicknesses of 1 mm. each (from 1 to 8 mm.) was roentgenographed at the same time for densitometric measurements. Finally, vertebrae decalcified to various degrees were placed under the patients' back alongside the spinal column and roentgenographed together with the patients' spines.

It was determined that the first roentgen sign of demineralization in an isolated vertebra is demonstrated when the calcium loss reaches 3 per cent of the normal value. A similar change in the spine of the living individual, however, can be demonstrated only after the calcium loss reaches approximately 60 per cent of the normal value.—*T. Leucutia, M.D.*

Fusi, Giorgio. Considerazioni e rilievi in tema di osteoporosi con particolare reguardo alle alterazioni scheletriche senili; studio radiologica e biochimico di un gruppo di 20 vecchi. (Considerations and investigations on the subject of osteoporosis with particular attention to senile skeletal alterations; radiological and biochemical study of a group of 20 aged persons.) *Radiol. med.*, March, 1953, *39*, 209–242.

Babaiantz was the first to call attention in 1947 to the necessity of distinguishing between the histologic and roentgenologic concept of osteoporosis. Mack, Brown and Trapp (see this Journal, 1949, 61, 808–825) have determined experimentally that of the various components of the bone, calcium is responsible for approximately 79.60 per cent of the roentgenological absorption, phosphorus for 14.8 per cent, oxygen for 5.5 per cent and carbon for 0.1 per cent, whereas the organic substances, including ossein and fat, account for the remaining 2 per cent.

Following this introduction the author in the first part of the article discusses certain problems of physiopathology especially as regards the role of the organic matrix and of the osteoblasts in producing absorption of the bone. Of capital interest is the intimate and very complex interrelationship which exists between the osseous skeleton and several of the glands of internal secretion. Owing to the vastness of the subject, the author limits himself to an analysis of the influence of only two glands, the gonads and the adrenals. He refers extensively to the many important publications found in the literature and attempts to coordinate the several theories suggested by the various investigators.

Based on such analysis he proposes the following schematic classification of generalized osteoporosis: (A) *osteoblastic:* (1) hormonal: (a) senile, (b) postmenopausal, (c) due to ovarian agenesis; (2) due to immobilization; (B) *humoral:* (1) due to protein de-

ficiency, (2) due to excessive transformation of proteids into glucides (osteoporosis in Cushing's syndrome and in acromegaly), (3) due to excessive protein catabolism (osteoporosis in hyperthyroidism).

In the second part of the article, the author presents the results of his investigations in 20 old persons whose ages varied between sixty and ninety-five years. These investigations consisted of systematic roentgenographic examination of the entire skeleton and of blood chemistry studies, including calcium, phosphorus, protein, alkaline reserve and nitrogen determinations. The 20 cases are arranged tabularly, by listing the sex, age, antecedents, presence of accessory calcifications, blood chemistry findings and roentgenographic findings of the skeleton.

The author arrives at the conclusion that the skeletal changes in aged persons consist essentially of senile osteoporosis of the osteoblastic type which on the roentgenogram manifests itself as a simple atrophy of bone. This conclusion is contrary to the dual theory of many investigators who hold that the alterations observed in the diaphyses of long bones are senile degenerative changes whereas the senile osteoporosis affects electively the spongy bones. Such view of the subject is due to a confusion between the histologic and roentgenologic concept of osteoporosis. The fact is that in both instances the increased radiotranslucency is the result of a decrease in the total mass of the bone as demonstrated histologically (and not to a decalcification), and that consequently the process will become manifest earlier on the roentgenograms of the less dense spongy bones than on the roentgenograms of the more dense compact bones. The author states, however, that the etio-pathogenesis of senile osteoporosis is very complex and that a simple atrophy of the bone is often associated with either osteomalacia or Paget's disease. According to Turano this latter manifestation may be considered as a compensatory reaction to deficient bone apposition incidental to age.—*T. Leucutia, M.D.*

Wilson, Margaret E., and Stowell, Robert E. Cytological changes following roentgen irradiation of the liver in mice. *J. Nat. Cancer Inst.*, April, 1953, *13*, 1123–1137.

Doses of roentgen irradiation up to 12,000 r (1 cm. depth within the animal) were delivered to the liver region of mice, the rest of the body being shielded.

The livers were studied one, two and three days after irradiation. Chalkley ratio measurements showed a decrease in cell size, due principally to a decrease in lipid content. Usually both nuclei and nucleoli were larger than in the normal liver cells and the nucleo-cytoplasmic ratio was increased.

The fat in the fasted irradiated mouse liver was found in the cells at the center of each lobule, whereas there was little or no fat in the cells near the portal areas. This was in sharp contrast to the fasted non-irradiated controls. Apparently the cells at the periphery of the lobule are more sensitive to irradiation effects and this may be related to higher oxygen tensions at these areas of the lobule. There is apparently an interference with lipid metabolism and possibly other fundamental functions of these liver cells. —*Chauncey N. Borman. M.D.*

Abramson, Daniel, Caton, William L., Jr., and Roby, Charles C. The effect of relaxin on the excretion of diodrast in the castrate hysterectomized rabbit. *Am. J. Obst. & Gynec.*, March, 1953, *65*, 654–659.

Relaxin was first isolated and described by Hisaw, who showed that this substance was responsible for the relaxation of the pelvic ligaments in pregnancy. The substance has been prepared from whole ovaries of sows, the uterus, placenta and blood serum of other mammals, and from the blood serum of pregnant women. Recent attempts to extract it from human placenta have not been successful.

Intravenous pyelograms were taken of rabbits prior to and after hysterectomy and castration, again after ethinyl estradiol administration, and again following the administration of relaxin. The pyelograms taken after relaxin administration showed delay in complete filling of the ureters and appearance of the opaque medium in the bladder comparable to that seen in the pregnant rabbit. Intravenous pyelograms were made of a pregnant rabbit on the twenty-second day of gestation as a control.

Animal experimentation on the ureter at best is most difficult. The delay in ureteral and bladder filling is believed to be due to an atonicity of the ureteral musculature caused by estradiol relaxin therapy.—*Paul R. Dirkse, M.D.*

Schneider, David H., Eichner, Eduard, and Gordon, Maurice B. An attempt at production of hydronephrosis of pregnancy, artificially induced. *Am. J. Obst. & Gynec.*, March, 1953, *65*, 660–665.

There has always been some controversy as to whether the hydronephrosis associated with pregnancy is caused by hormonal changes, pressure phenomena, or both. In an attempt to prove or disprove the hormonal factor, it was believed that if a nonpregnant woman in the childbearing period could be given sufficient hormones of the type produced in the body by pregnancy, perhaps the side effect of pregnancy affecting the urinary tract could be produced without the pressure factor of a large uterus.

A considerable number of previous articles are quoted from the literature with rather conflicting conclusions.

The material presented includes experiments on eight nonpregnant women, all of childbearing age. These were given, after thorough preliminary exam-

inations, estradiol pellets, progesterone and chorionic gonadotrophic hormones in an attempt to reproduce natural hormonal secretion by the body during pregnancy. Intravenous pyelograms were taken at intervals. These were not successful in showing the hormonal effect on the ureters demonstrable by pyelography. (Relaxin was not used.)

The authors conclude that the amount and/or quantity of the hormones given, for the length of time used, were insufficient to produce any definite ureteral changes. They believe that the specific hormone was not given (it may not be known yet), or that the quantity of hormone was insufficient and hope to be able to demonstrate this by later experiments.—*Paul R. Dirkse, M.D.*

Montgomery, P. O'B., and Warren, Shields. Mechanisms in acquired radioresistance of cancer. *Radiology*, March, 1953, *60*, 421–424.

The authors transplanted, subcutaneously, Gardner mouse lymphosarcoma 6C3HED from mouse to mouse in order to test any acquired radioresistance of this tumor to further irradiation. Roentgen irradiation was done with a G-E Maximar Therapy apparatus at 200 kv., with 3 mm. Al inherent filtration, target distance of 35.5 cm. and an output of 165 r/min. The tumor tissue was irradiated in test tubes before each transplant.

The lethal "in vitro" single dose of this tumor was found to be in the neighborhood of 4,500 r. By gradually increasing the single "in vitro" dose in sublethal quantities before successive transplants, the authors again found the single lethal dose to be about the same as in the nonirradiated tumor, despite an accumulated irradiation quantity of nearly twice the lethal dose. Hence, they could not demonstrate any increased resistance to roentgen rays. Comparative histological study did not reveal any difference in the general cellular morphology between the nonirradiated and the progressively irradiated tumor.

After a brief discussion of these findings in relation to the theories of the mechanism of acquired radioresistance, the authors conclude that this is probably the result of an alteration of the host-tumor relationship secondary to the host's reaction to the irradiation, rather than an intrinsic change in the irradiated tumor.—*Dean Nichols, M.B.*

Chamberlain, Richard H. The place of physics in clinical radiology; Carman Lecture. *Radiology*, March, 1953, *60*, 331–347.

In this 1952 Carman lecture, the author discusses and reviews the scope of physics in medical radiology.

In producing the utmost in diagnostic accuracy, a basic knowledge of the voltage and milliampere range of power supplies, timing circuits, advances in tube design, and the geometry of roentgen-ray projection is essential. From applied physics, the desitometer aids accurate standardization of photographic emulsions and development. The limitations of visibility of objects as to outline, brightness and size have thus been determined quantitatively. Fluoroscopic amplification by the Coltman tube and by electronic circuits using the orthicon television tube is ready for clinical trial.

In roentgen therapy, the precise physical calibration of dose rate, half-value layer, field uniformity, depth dose and isodose contours are accepted as essential. The magnitude of potential errors and safety measures should never be minimized. The volume or integral dose deserves more consideration since this is a more true representation of ionization in tissue. Energy absorption of various tissues is significantly different at certain qualities of radiation.

Radium and radon therapy is more complex and one must be wary of errors from faulty commercial calibrations, leakage, and packing. Experience with large doses of radium in carcinoma of the cervix shows an improvement in cure rates. However, complications occur more than twice as often in those receiving 5,000 or more milligram hours. Orthographic projections of radium distribution will allow physical calculation of roentgens delivered to important adjacent organs.

In using radioactive isotopes, one must be conversant with the chemical and physical forms, half-life, types of emissions, decay products, and other specific data of the individual isotopes. In quantitative determinations of distribution, one must use variations of the Geiger-Müller apparatus, ionization chambers, scintillation instruments, and photographic methods such as radioautography. An understanding of the principles and design of these systems is necessary in order to choose and use the appropriate method. The quantitative accuracy is, at present, less than in most standard methods, and the cooperation of an informed physicist is advisable.

The bulk of radiation therapy is still properly accomplished by conventional methods. These should not be discarded until the worth of newer techniques has been verified. By working in coordination with physicists and becoming familiar with the applied aspects of this field, radiologists will enhance their own accuracy, efficiency and prestige.—*William A. Goodrich, Jr., M.D.*

Fullenlove, Tom M. Recording timer for arteriography. *Radiology*, March, 1953, *60*, 428–429.

The author describes a simple clock, electrically driven, with a dial holding lead numbers so placed that its circumference extends beyond that of the clock proper. Projecting beyond the dial is an oval wire containing a pointer. The clock is placed in such a way that the image of the projecting dial with its pointer is recorded on the exposed film. An electric switch is closed at the beginning of the injection for an arteriogram, setting the dial in motion.

Each successive film then has a permanent time mark, recording the time-interval after the beginning of the injection of the opaque medium.—*Dean Nichols, M.D.*

Seldinger, Sven Ivar. Catheter replacement of the needle in percutaneous arteriography; a new technique. *Acta radiol.*, May, 1953, *39*, 368–376.

Angiography by injection of the contrast medium through a catheter has the following advantages over injection through a needle:

1. The contrast medium may be injected at any level desired.
2. The risk of extravascular injection of the contrast medium is minimized.
3. The patient may be placed in any position required.
4. The catheter may be left in situ without risk while the films are being developed, thus facilitating re-examination if necessary.

A new method for percutaneous intro duction of a catheter permits the use of a catheter and needle of the same size, thus assuring that the hole in the artery is no larger than the catheter. This is accomplished by passing a flexible leader through the needle, after the percutaneous puncture of the artery, then removing the needle, and feeding the catheter over the flexible leader. The leader can then be removed and the catheter advanced to the desired level.

The technique is simple and has been used in 40 cases, of which 35 were aortographies via the femoral route, 3 subclavian aortographies, and 2 catheterizations of the femoral artery in a distal direction. Resistance to the passage of the catheter or leader is a contraindication to advancement.—*Lois Cowan Collins, M.D.*

Lindsay, Duncan D., and Stern, Babette E. A new tissue-like material for use as bolus. *Radiology*, March, 1953, *60*, 355–362.

Bolus material is generally accepted as needed in beam therapy to give a regular shape to the body surface so that physical calculations of dose may be clinically applied. Rice, soda, wax and water all have disadvantages. A newly developed material produced by English candy manufacturers for the Lincolnshire Radiotherapy Centre approaches the ideal. It is made in constant sized spheres 2.3 mm. in diameter and consists by weight of 87 per cent sucrose and 13 per cent magnesium carbonate levis. Packing variations are absent, so bags should be pressed into position as firmly as possible. No amount of pressure will cause undesired high density. Air interstices are insignificant. The electron density and effective atomic number are within 2 per cent of human tissue at all qualities of radiation. The material is undamaged by rough usage, high humidity and body temperature.—*William A. Goodrich, Jr. ,M.D.*

Marr, J. T. A method of detecting a questionable film artifact. *Radiology*, March, 1953, *60*, 425–427.

The author describes a method by which contact type of film artifacts can be detected when other methods fail. The method consists primarily of the removal of a small amount of emulsion from each side of the film and comparison of light transmission through two areas.—*A. Ralph Waston, M.D.*

Ernst, Edwin C., Ernst, Edwin C., Jr., and Ernst, Roland P. Plastic vaginal cylinder; accessory to the expanding cervico-uterine radium applicator. *Radiology*, April, 1953, *60*, 583–587.

The authors describe a method of irradiation of carcinoma of the uterine cervix, using a plastic vaginal cylinder as an accessory to the expanding cervicouterine radium applicator.

The applicator with cylinder attached is illustrated, and methods by which it is used and dosages computed are described.

Evidence is presented to show that the method has advantages, as evaluated by the 10 clinical and physical criteria proposed by the authors: simplicity, flexibility, reliability, uniformity of dose, control of radium sources, correction of deformities, protection of normal structures, self-protection, predetermined dosage measurements, and duplication of the radiation procedures.—*Lynne J. Taylor, M.D.*